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Affinity adsorption

Removal of pharmaceuticals at the source

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Summary

Many pharmaceuticals are present in urine and feces and end up in wastewater via the toilet. Sewage treatment plants (WWTPs) in general have not been designed to remove pharmaceuticals, and appear to remove only about 70 % of the total amount of pharmaceuticals. The remaining pharmaceuticals are discharged into surface water. This may negatively affect the aquatic environment and the production of drinking water.

Adsorbents like activated carbon may be used to remove organic micropollutants like pharmaceuticals from water, but their efficiency is decreased by the presence of natural or effluent organic matter. These OM compounds, which are present in concentrations in the order of magnitude of mg/L (whereas micropollutants are only present in µg/L) compete with the micropollutants for adsorption sites, thus reducing the adsorption capacity of the adsorbent for micropollutants. Pharmaceuticals always contain functional groups in their molecular structure. These can be used for specific interactions with compounds present at the adsorbent surface. In a previous project (Hofman-Caris et al., 2015) it was shown that when adsorbents, which can show such interactions are applied, competition with other organic compounds is prevented. However, the adsorbents used in that project were too expensive for large scale applications. Therefore, in the present project we tried to find a more cost effective carrier material and surface modification.

Several materials were tested, and finally Ankerfume M25 (a a relatively cheap and inert carrier material) modified with silane Dimethyl octadecyl [(3-trimethoxy silyl)propyl] ammonium chloride was chosen as an appropriate adsorbent for diclofenac. The preparation of this adsorbent was optimized for diclofenac adsorption, but experiments showed that also bezafibrate, gemfibrozile, sulfamethoxazole, ketoprofen, naproxen and salicylic acid can be adsorbed by this adsorbent, as had been expected based on their molecular structure. A maximum adsorption capacity of about 40 mg diclofenac per g of adsorbent was observed, both in drinking water and in artificial urine. Taking into account the number of surface active groups present according to TGA-analysis, this means that about 87 % of these functionals groups is loaded with diclofenac, which shows the high effectiveness of the adsorbent. Furthermore it was shown that adsorption occurs almost instantaneously, and that in a (waste)water matrix it seems to be irreversible.

Two pilot investigations were carried out: one in the university hospital UMC in Utrecht, and one in the office buildings of the Limburg Water Authority and the Water Authority Company Limburg. In all cases people were asked to add adsorbent to the toilet whenever they used it. In the hospital it was found that many people, both staff and patients, were not aware of the fact that pharmaceuticals may enter the environment by the toilet. However, when they realized this, many were willing to cooperate and add the adsorbent to the toilet when using it. Also in the rinsing kitchen (for bedpans) the adsorbent pellets were used frequently. Samples of the hospital wastewater were taken for adsorption experiments. In this wastewater the diclofenac adsorption capacity appeared to be lower than in drinking water or artificial urine, which probably was

caused by the simultaneous adsorption of other compounds from the wastewater, but still significant adsorption could be observed.

Also in the office buildings the people were very willing to cooperate with the pilot investigation and to use the adsorbent. Unfortunately, due to large differences in the wastewater samples taken here it was not possible to measure the effect of the use of the material, as the fluctuations in concentrations were too large.

It was concluded that it is possible to prepare an efficient adsorbent for specific compounds/pharmaceuticals, using a relatively cheap and inert carrier material, modified with a specific silane. And it was shown that people are willing to use such an adsorbent in order to protect the environment from pharmaceuticals.

Practical and cost effective dosing forms for application of the adsorbent in homes, hospitals, offices etc. still have to be developed. However, application of the adsorbents in large scale WWTP processes might also be a possibility.

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Contents

1 Introduction

In urbanised area's the quality of water used for the production of tap water is coming under pressure due to increased amounts of anthropological contamination (Kümmerer 2010, Pedrouzo et al. 2011, Sanderson 2011, Bäuerlein et al. 2017, Hofman-Caris et al. 2017, Van Wezel et al. 2017). Among these contaminants are the so called micropollutions of which pharmaceuticals make up a large part. The rise in the pollution in combination with an increase of the average life expectancy leads to mounting use of the said. These pharmaceuticals will filter into surface waters mainly through sewage treatment plants (STP) (Ternes 1998, Bäuerlein et al. 2012, Bäuerlein et al. 2012, Hofman-Caris et al. 2015, van Wezel et al. 2017, Bai et al. 2018, Brunsch et al. 2018, Česen et al. 2018, Miller et al. 2018). As surface waters often are used as sources for drinking water, drinking water companies face the challenge to remove these compounds. So far, the removal efficiency of the treatment techniques employed is high enough to ensure a high tap water quality. However, the expected raise in concentrations will increase pressure on the treatment techniques. Furthermore, the ecological impact of the pharmaceuticals on the ecosystem needs to be considered. For this reason some sewage treatment plants (STPs) have already installed a fourth treatment step (Knopp et al. 2016, Soltermann et al. 2016, Bourgin et al. 2018), such as ozonation and/or activated carbon. The advantage of these treatment steps is that the amount of micropollutants released into the environment can be reduced, which will make it easier for water companies to produce consumable tap water. However, installation of a fourth treatment is pegged to increase costs and in some cases the ecological benefits might not justify the costs in the eye of the public. Furthermore, the efficiency of the fourth treatment will depend on the type of technology implemented. Therefore, better or new ways to use already existing treatment steps for wastewater treatment, is an alternative approach.

In this report we propose such an approach with the aim to remove a pharmaceutical, that is ubiquitously present, from sewage. The proposed method will make use of the already existing treatment step, specifically the sedimentation process. We developed an benign adsorption material that predominately adsorbed diclofenac. This material can be added to the water stream directly at the source of the contamination, the toilet, where a limited number of contaminants is present, the concentration of the compound is still high and a maximum of the pharmaceutical will be adsorbed. The toilet remains the main gate way into the aquatic environment for pharmaceuticals, either through urination or disposal of out-of-date medicines. The turbulence in the toilet water also ensures good mixing during flushing providing a good contact between compounds and adsorbent, which favours the adsorption process. In this report we will describe the synthesis of the material and its application in various water matrices in the laboratory. Furthermore, we tested the acceptance of such an adsorbent by the public by having patients, hospital staff and office employees use these adsorbents.

2 The principle of affinity adsorption

For this study “affinity adsorption” was applied (Hofman-Caris et al. 2015). The principle is based on highly selective interactions between the adsorbent surface and structural elements of the analytes. Especially for (classes of) pharmaceuticals, which were designed with special functional groups, this may be very efficient. The principle of affinity adsorption is shown in Figure 1. As adsorption is based on a specific interaction between surface and analyte, competition with other compounds present will be less important. Especially in e.g. urine and wastewater, where concentrations of organic compounds are relatively high, this is an advantage over e.g. the use of activated carbon.

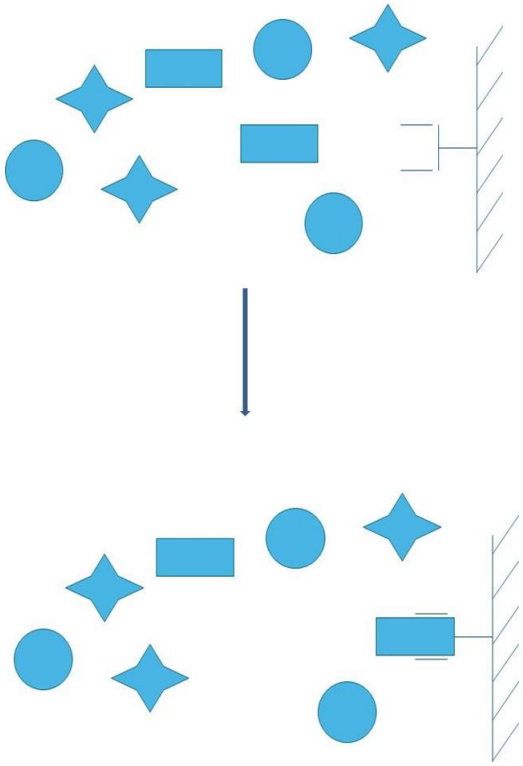


Figure 1: principle of affinity adsorption

In the previous research project the principle of affinity adsorption was shown using adsorbents with a polymer or silica carrier. Polymer carriers have three disadvantages:

- they are not commercially available at a large scale
- they are very expensive
- their density is in the same order of magnitude as the density of water, which makes removal of the loaded particles from wastewater “difficult”.

Therefore, in this project relatively heavy, cheap and non-toxic carrier materials were tested, with a particle size in the µm range, in order to make it easier to remove the material from water after use. Finally, aluminosilicate was chosen as a material with a relatively large surface area. This material contains surface OH-groups that may be used in surface reactions with functional groups like silanes. Thus, the particle surface can be functionalized for interactions with a specific material. As the material has a relatively high density, it will easily precipitate in the STP. Then it can be removed with the sludge or sand. In the Netherlands it is not allowed to use this sludge in agriculture, so it will have to be incinerated. This leaves the aluminosilicate material, which is harmless to the environment and human health.

Although reuse of the material may be considered, this was not part of the scope of the present investigation.

3 Materials and methods

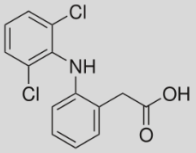
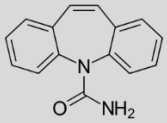
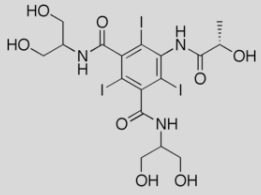
3.1 Chemicals and consumables

All analytes and salts (at least 98 % pure), dimethyloctadecyl[3-(trimethoxysilyl)propyl]ammonium chloride solution were obtained from Sigma-Aldrich (Zwijndrecht, The Netherlands). SiliaBond TBA chloride with particle diameter between 40 – 60 µm and a pore size of 60 Å was purchased at SiliCycle (Quebec, Canada). Ultra-pure water (Milli-Q water, Veolia, The Netherlands), with a resistivity of >18 MΩ was used for adsorption experiments when stated and for the preparation of artificial urine. Tap water was taken from a tap in the laboratory. The tap was allowed to run for a few minutes before the water was used. Glassware was cleaned to fulfil XRD standards. Syringe filters were Spartan 30/0.45 RC from Whatman (Dessen, Germany). Regenerated cellulose filters (0.20 µm) were bought at Phenomenex. Paper filters were bought from Whatman (Dessen, Germany). Ankerfume M25 (Sibelco, The Netherlands) is a aluminosilicate with a surface area of about 20 m^2/g. Other carrier materials used in this study were Kaolin SL-55 (see 0), Black Clay, Silverbond M600 crystalline silica (produced from high purity quartz feed stock with a specific surface area of about 4.2 m^2/g), and Sibelite M6000 (a high-purity silica produced from cristobalite by iron-free grinding and accurate sieving by means of air-separators, with a specific surface area of about 5 m^2/g), all supplied by Sibelco. Aluminosilicates are a major component of kaolin and other clay minerals.

Furthermore, experiments were carried out using commercial amorphous silica with a specific surface area between 475-560 m^2/g and pore size between 50-76 Å purchased from Sigma-Aldrich.

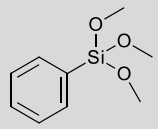
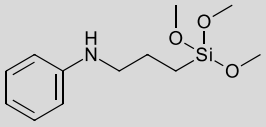
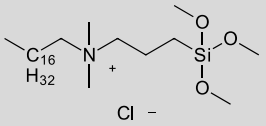
At the start of the project three pharmaceuticals were chosen. There structures are shown in Table 1.

Table 1: Composition of pharmaceuticals used in this project, and of silanes tested.

Name	Pharmaceutical structure
Diclofenac	
Carbamazepine	
Iopromide	

The composition of silanes used in this project is shown in Table 2.

Table 2: composition of silanes tested

Name	code	Silane structure	Producer
Trimethoxy phenyl silane	A		Sigma-Aldrich
Trimethoxyl silyl propyl aniline	B		Sigma-Aldrich
Dimethyl octadecyl [(3-trimethoxy silyl)propyl] ammonium chloride	C		Sigma-Adrich

3.2 Modification of carrier material

In order to realize chemical interactions at the adsorbent surface, the surface has to be modified with organic compounds, carrying active groups that can interact with other compounds. As the carrier material is an aluminosilicate, and as previous research (Hofman-Caris et al., 2015) had shown that silanes can be very effective to interact with other compounds, it was decided to modifiy the carrier surface using silanes. These can react with hydroxyl groups present at the particle surface, thus creating an active layer at this surface.

During the first experiments the silane solutions and carrier material were added to a Henschel FM 40 A mixer, and afterwards the material was dried. In the first experiments 1 and 3 wt % of silane was applied, washing with water/methanol (90/10 v/v) , filtration, drying for 1 hour at 80 ºC.

The stability of the modification was tested in desorption experiments. These were carried out by dispersing 100 mg of modified carrier material in 20 mL of water. The mixture was shaken overnight. The particles were removed (syringe filter) and the UV spectrum of the filtrate was recorded. Thus an indication was obtained about possible leakage of the material from the particle surface.

Subsequently carrier material (both on Ankerfume and silica) was modified with 10 and 15 % of silane, In order to remove unreacted material a washing procedure was developed. Six types of washing procedures were tested:

1. Washing with methanol (ratio 1:10), filtration, drying for 1 hour at 80 ºC
2. Washing with 1-butanol (ratio 1:10), filtration, drying for 1 hour at 80 ºC
3. washing with 2-propanol (ratio 1:10), filtration, drying for 1 hour at 80 ºC
4. washing with dibutyl ester DBE (ratio 1:10), filtration, drying for 6 hours at 120 ºC
5. washing twice with water (ratio 1:5), filtration, drying for 1 hour at 80 ºC
6. washing with H_20/MeOH (50:50)

Each of these materials (110 µg) was subsequently dispersed in 20 mL of MilliQ water and stirred overnight. The solid was removed with syringe filter from the liquid and the filtrate was subjected to UV analysis to check for residual silane on the material.

As the adsorbent that was selected for further experiments may eventually be used in commercial applications, a name for the concept was invented: “CatchAmed”.

3.3 Adsorption experiments

For the lab scale adsorption experiments with diclofenac in drinking water, artificial urine, and wastewater Ankerfume A25 was used, modified with 15 % of silane C, and washed according to procedure 5.

For pilot experiments modification of Ankerfume was carried out on a larger scale. The Ankerfume and silane solution were added to the Henschel FM 40 A mixer - 10 kg of the Ankerfume A25 was mixed with 3.57 kg silane C 42 % solution in methanol, resulting in 15 % silane in the final product. Subsequently the mixture was mixed twice for 5 min at 1740 rpm. After that, the solid was separated from the liquid phase and put into oven for drying at 90 ºC. Next the material was washed with water and dried again at 90 ºC.

3.4 Pelletization of adsorbent

Sibelco tried to pelletize the Ankerfume M25 material. For unmodified carrier material it appeared to be possible to pelletize it into pellets of about 0,76 g (see Figure 2 and Table 6). However, modified Ankerfume M25 with 15 % of silane C appeared to be very hydrophobic and thus couldn’t be pelletized. It was tried to improve the pelletization by adding a salt or carboxymethyl cellulose, a compound which is also used for the pelletization of pharmaceuticals, but that didn’t improve the pelletization results. For the pilot study at the UMC hospital these pellets, however, still were used, as here the main aim of the pilot was to determine whether people are willing to add something to the toilet. For the pilot study at the office building, the adsorbent was used as a powder.

Figure 2: Pellets of unmodified Ankerfume M25

3.5 TGA experiments:

Thermogravimetric analysis was carried out in order to determine the amount of organic material present at the adsorbent surface. In this way the concentration of active groups at the surface could be calculated. Thermogravimetric experiments were performed using a TGA/DSC+ from Mettler Toledo (Breda, The Netherlands). The total gas flow was set to 70 mL N_2. The programme started at 120 ºC and the temperature remained constant for 65 min to remove residual water. Afterwards the temperature

was raised to 700 ºC at a rate of 20 K/min. The data was evaluated using the Stare software V16.00 and exported to GraphPad Prism 5 (La Jolla, CA) for further evaluation.

3.6 Preparation of artificial urine

Artifical urine was prepared based on literature values (Lai et al. 2017, de Wilt 2018). For the preparation compounds mentioned in Table 2 were dissolved in 25 L of MilliQ water. The composition of artificial urine is shown in Table 3.

Table 3: Salt concentrations in MilliQ water for the artificial urine experiments.

Compound	mg/L
L+ Lactic acid	19.3
citric acid	76.6
$NaCO_3$	420.2
Urea	2044.0
$CaCl_2.2H_2O$	46.7
NaCl	1052.4
$MgSO_4.7H_2O$	49.8
$NaSO_4$	284.6
KH_2PO_4	189.9
K_2HPO_4	241.9
NH_4Cl	267.1

3.7 Sorption Models

For a system consisting of a sorbent and an aqueous phase, several models, e.g. , Langmuir and Freundlich, can describe the equilibrium between the solute's aqueous concentration (C_w) and the concentration on the sorbent (C_s). The ratio (1) between concentrations on the sorbent and in the aqueous phase is the adsorbent-water distribution coefficient K_D expressed in L/kg:

$$K_D = \frac{C_s}{C_w} \quad (1)$$

For this project, we selected one mathematical model to describe sorption behaviour. Langmuir isotherms were chosen to receive information on the sorption capacity of the adsorption material as well as the sorption kinetics. The Langmuir equation assumes that the sorbent has a limited number of sorption sites with similar affinity. When the concentration increases, the sorbent gets saturated when a maximum concentration on the sorbent is reached (C_{max}). The parameter K_L is a constant reflecting the equilibrium of the sorption process.

$$C_s = \frac{K_L \cdot C_{max} \cdot C_w}{1 + K_L \cdot C_w} \quad (2)$$

In this model at low C_w ($C_s \ll C_{max}$) K_D is constant. All log K_D values mentioned in this paper are calculated using equation 3 which is derived from equation 2 and 1.

$$K_D = K_L \cdot C_w \quad (3)$$

3.8 Adsorption experiments

3.8.1 Measurements

For the single compound experiments 40 mL glass vials were filled with 20 mL of an unbuffered solute solution to which the adsorbent was added. The starting concentration of the solution was around 10 mg/L. The amount of sorption material varied between 1 and 100 mg, depending on the expected sorption affinity that was determined in preliminary experiments. Vials with these suspensions were rolled on a Stuart Roller mixer at rate for 15 h (overnight) at 20 ºC. Subsequently 20 mL of of the suspension were filtered through a syringe filter. The filtrate was analysed immediately with UV/vis spectrometry (Unicam UV500, ThermoScientific) in 10 mL cuvettes. The spectra were recorded from 200 -400 nm (120 nm/min) using VISIONpro. In preliminary experiments it was established that the adsorption equilibrium was obtained within 2 h. Procedural blanks (i.e. pure water containing solutes without sorbent) revealed that no other material than the adsorbents involved in these experiments adsorb relevant fractions of the solute. Procedural blanks were treated in the same way as samples with sorption material. Concentrations in the blanks were compared to concentrations in the spiking solution and the values were coincident with a deviation of approximately 5 %, meaning the solutes do not adsorb to the vials or syringe (filter), nor are other compounds released that interfere with the solutes.

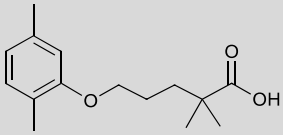
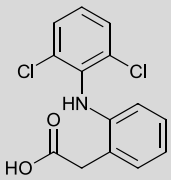
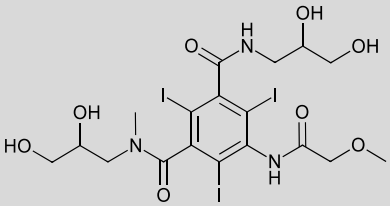
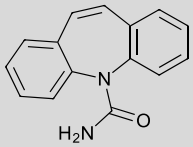
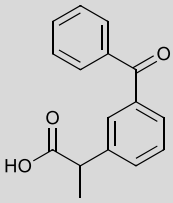
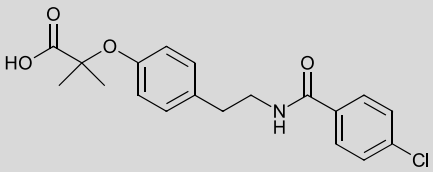
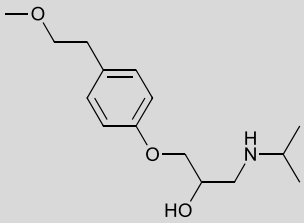
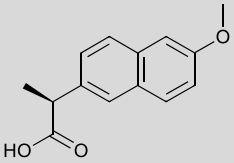
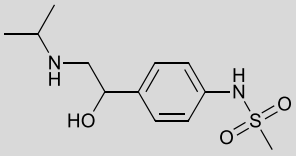
For the multi component experiments in artificial urine (see SI for details) 300 mL glass flasks were filled with 250 mL of the unbuffered solute solution in artificial urine. The concentration of the solute varied between 110 and 500 µg/L The amount of sorption material varied between 2 and 500 mg. Vials with these suspensions were shaken for 15 h (overnight) at 20 ºC. Subsequently the 250 mL was filtered through a Wattman cellulose nitrate filter (0.45 µm). The filtrates were analysed the next day with a TSQ Vantage (ThermoScientific, The Netherlands). Procedural blanks (i.e. pure water containing solutes without sorbent) revealed that no other material than the adsorbents involved in these experiments adsorb relevant fractions of the solute. Procedural blanks were treated in the same way as samples with sorption material.

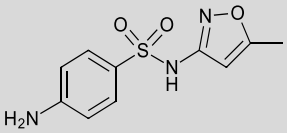
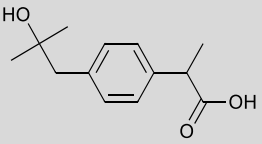
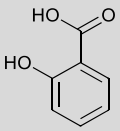
The diclofenac experiments in sewage were performed in 300 mL flasks as follows. Firstly the sewage was filtered through a folded paper filter to remove larger particles and suspended matter. The filtrate was spiked with diclofenac to yield a concentration of 425 µg/L. To a solution of 250 mL various amounts of adsorbent were added (3 – 700 mg). The suspensions were shaken overnight for 15 h at 20 ºC. Subsequently, the suspensions were filtered through a cellulose nitrate filter to remove the adsorbent. Next the internal standards were added and solution was filtrated through a generate cellulose filter (0.2 µm) and analysed using a TSQ Vantage.

For experiments in artificial urine the pharmaceuticals listed in

Table 4 were used.

Table 4: Pharmaceuticals and one metabolite tested in artificial urine.

		Molecular mass	Charge at pH ≈ 7
Gemfibrozil		250,333	-1
Diclofenac		296.148	-1
Iopromide		791.112	0
Carbamazepine		236,27	0
Ketoprofen		254,281	-1
Bezafibrate		361.819	-1
Metoprolol		267,364	1
Naproxen		230,259	-1
Sotalol		272,365	1

Sulfamethoxazole		253.279	-1
2-hydroxy ibuprofen		222.284	-1
Salicylic acid		138,121	-1

The structural properties of some pharmaceuticals that resemble diclofenac are shown in Table 5.

Table 5: Structural properties of the carboxylic pharmaceuticals. Calculations were performed using Chemicalize.org.

	Diclofenac	Ketoprofen	2-hydroxy ibuprofen	Salicylic acid	Naproxen
Van der Waals volume Å^3	236.85	233.68	220.45	118.30	213.06
Van der Waals surface area Å^2	360.28	367.50	370.25	182.25	343.72
Solvent accessible surface area Å^2	424.95	452.27	426.90	283.96	452.50
Topological polar surface area Å^2	49.33	54.37	57.53	57.53	46.53
Minimum projection area Å^2	40.96	41.68	35.53	23.03	34.77
Maximum projection area Å^2	78.63	72.81	65.40	46.55	72.19
Minimum projection radius Å	4.62	4.37	3.70	3.56	3.92
Maximum projection radius Å	6.34	6.58	6.52	4.73	7.30

3.8.2 Software and model

Fits for the Langmuir and double Langmuir isotherms were calculated with GraphPad Prism 5 (La Jolla, CA).

The adsorption isotherms (Langmuir) were plotted using the GraphPad Prism. The following equation (3) has been used to receive the maximum sorption capacity (C_{max}) and the sorption coefficient K_L. C_s is the concentration on the adsorption materials and C_w the concentration the aqueous phase. More information on this sorption model can be found elsewhere.(Bäuerlein et al. 2012, Hofman-Caris et al. 2015)

$$C_s = \frac{K_L \cdot C_{max} \cdot C_w}{1 + K_L \cdot C_w} \quad (3)$$

3.9 Recovery experiments

For the recovery experiment a solution of 9,826 mg/L diclofenac in a L tap water was prepared. To this solution 737 mg of the adsorbent was added. The suspension was left stirring overnight for 15 h. The solution was subsequently separated from the solids by

filtration. UV/Vis spectrometry was used to establish that no diclofenac was left in the solution. The solid was dried in the oven overnight (35 ºC). 360 mg of the adsorbent were recovered and added to 490 mL of tap water. The suspension was stirred for 15 hours. After 5 h and 15 h samples were taken and measured for the presence of diclofenac released from the adsorption material.

3.10 Dispersion experiments

During pilot experiments it was observed that the adsorbent may attach to ceramics and glass. This problem may be solved by applying the adsorbent as an aqueous dispersion. For stabilization of this dispersion a surfactant will be required, but this surfactant shouldn't interfere with the adsorption of pharmaceuticals at the particle surface. Thus, some dispersion experiments, using different types of surfactants, were carried out, to check the effect of the presence of the surfactant on the adsorption capacity of the material. For the dispersion experiments a stock solution of 12.54 mg/L diclofenac in DW was prepared and the UV spectrum was recorded. From this solution two solutions were prepared. To one solution sodium dodecyl sulfate (SDS) was added (~200 mg/L) and to the other one cetyltrimethylammonium bromide (CTAB) was added (~54 mg/L). Also the UV spectra of these solutions were acquired. Subsequently, 270 mg of Ankerfume M25 15 % was added to 430 mL of each of these solutions. These suspensions were shaken overnight, the Ankerfume was removed by means of a syringe filter and the UV spectrum of the filtrate was recorded.

3.11 Pilot trials

In March a pilot study was carried out at two nursing wards (D4 and D5) of the UMC hospital in Utrecht. In all toilets, both for patients and staff and in the rinse kitchens for bedpans, containers with adsorbent were placed, as shown in Figure 3. Unmodified Ankerfume was used for these trials, as it appeared to be impossible to prepare stable pellets of the right size in time. For patients it was thought to be easier to use pellets than to dose a powder.

Next to the containers information was posted on the purpose and aim of the trial and the dosing. This information also was distributed in patient rooms, and during staff coffee breaks the project was explained.

Figure 3: CatchAmed at toilets of nursing wards in the UMC Utrecht

The weight of the pellets was determined, and the results are shown in Table 6. There was a relatively broad size distribution of the pellets, and therefore also the average weight of a selection of relatively small and of relatively large pellets was determined.

Table 6: Average weight of the pellets.

	Number of pellets	Total mass (g)	Average mass (g/pellet)
All pellets	135	101.31	0,75
	107	74.1	0,69
	60	49,58	0,83
	137	94,22	0,69
	132	97,29	0,74
	48	40,46	0,84
Small pellets	25	14,66	0.59
Large pellets	25	40,64	1.63
Overall			0,76

In the rinsing kitchen at ward D4 pellets were placed next to one po rinser. There also appeared to be a second po rinser at D4, so after two days the pellets were placed here too, but consequently for a shorter period. Similarly, pellets were placed in the rinsing kitchen of ward D5 two days later than on the toilets.

For the pilot at WBL/WL the same procedure was followed, but in this case modified powder could be used (Figure 5), and people were asked to add one spoon of powder each time they visited the toilet (see Figure 4). The volume of the spoon was about 1 ml, which would correspond to a volume of adsorbent that would be sufficient for the amount of diclofenac excreted by a person during toilet use. Furthermore, they were asked to keep a score if they had used the toilet to find out how many times the toilet

was really used (compared to the use of the powder). It could not be registered if people didn't do both things.

Figure 4: 1 ml spoon with round bottom

In both cases surveys were carried out among the staff, and also reactions of patients were collected.

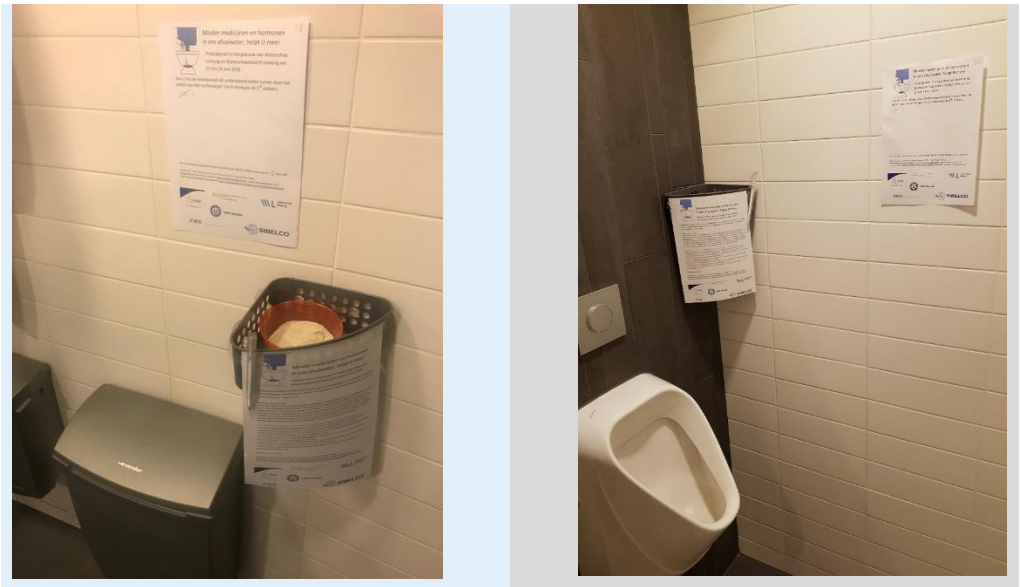


Figure 5: Pilot in the office building van WBL/WL in Roermond.

3.12 Sample collection during pilot trials

Sewage samples were taken at the university hospital UMC of the University Utrecht. Both nursing wards discharge on the same sump, which also is used for the rest of the seven story building. Grab samples of several litres were taken from this pit and stored in 5 L polypropylene jerry cans. A 24 hour average sample was taken, and in total 10 L of sample was taken, both on March 20th and March 22nd.

The office building of WBL and WL in Roermond is composed of two parts, which both discharge into a separate sump. Both sumps were sampled on Tuesday and Thursday, firstly in the week before the pilot trial and secondly during the pilot trial (May 15th,

17th, 22nd and 24th respectively). The pilot trial lasted for one week. The “new” part of the building discharges into a sump located in the Maria Theresialaan (see Figure 6). Here hourly grab samples were taking both during the morning and the afternoon. The grab samples taken at 8, 9, 10, 11 and 12 o’clock were mixed, and the grab samples taken at 13, 14, 15, 16 , 17 en 18 o’clock were mixed. The “old” part of the building discharges into a sump located at the side of the office, located at the Kapelaan Sarsstraat. Here mixed samples were taken during morning and afternoon (see Figure 7). In all samples diclofenac concentrations were measured.

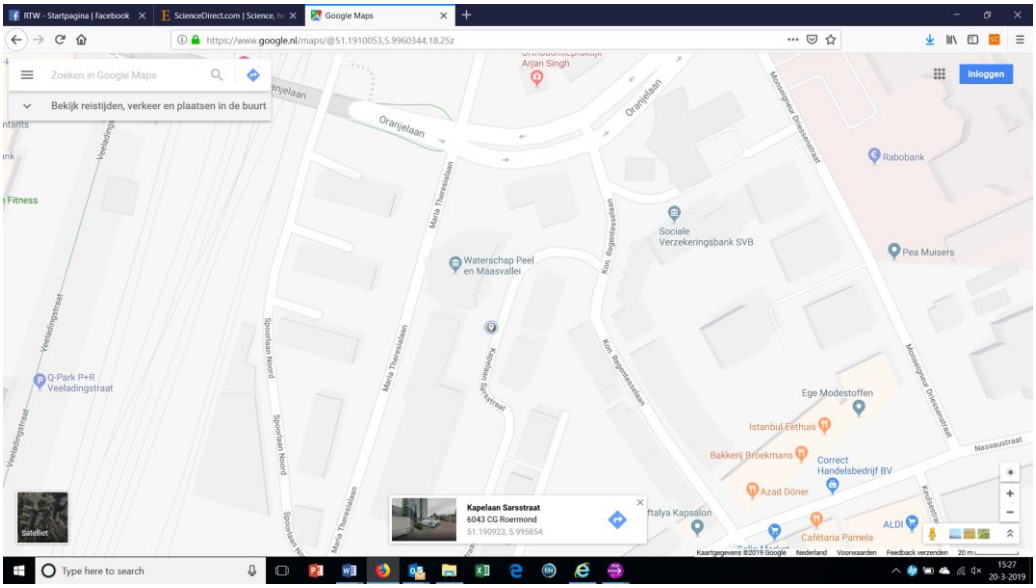


Figure 6: location of office building in Roermond (Google Maps)

Figure 7: Sampling at WBL/WL in Roermond

4 Results and discussion

4.1 Choice of pharmaceuticals and surface modification

Three pharmaceuticals were selected. Carbamazepine and diclofenac are known for their presence in STP effluent, and they are expected to have negative effects on the aquatic environment and possibly human health. Iopromide is not expected to be very toxic, but it is extremely difficult to remove in water treatment processes.

In previous research we obtained good results using affinity adsorption for both diclofenac and carbamazepine, by realizing a charge interaction for diclofenac and a π-π interaction for carbamazepine at the particle surface (Hofman-Caris et al. 2015). For iopromide no effective adsorbent has been described yet in literature. It was decided to apply silane A to obtain π-π interactions between the carrier material and carbamazepine, and silane C to obtain an interaction between the positively charged silane at the carrier surface and the negatively charged diclofenac molecules. It was hoped that iopromide might either be adsorbed by charge interaction or by π-π interaction.

Furthermore silane B was applied as it contains both a phenyl and an amine group, and thus might interact with the pharmaceuticals selected.

4.2 Desorption experiments

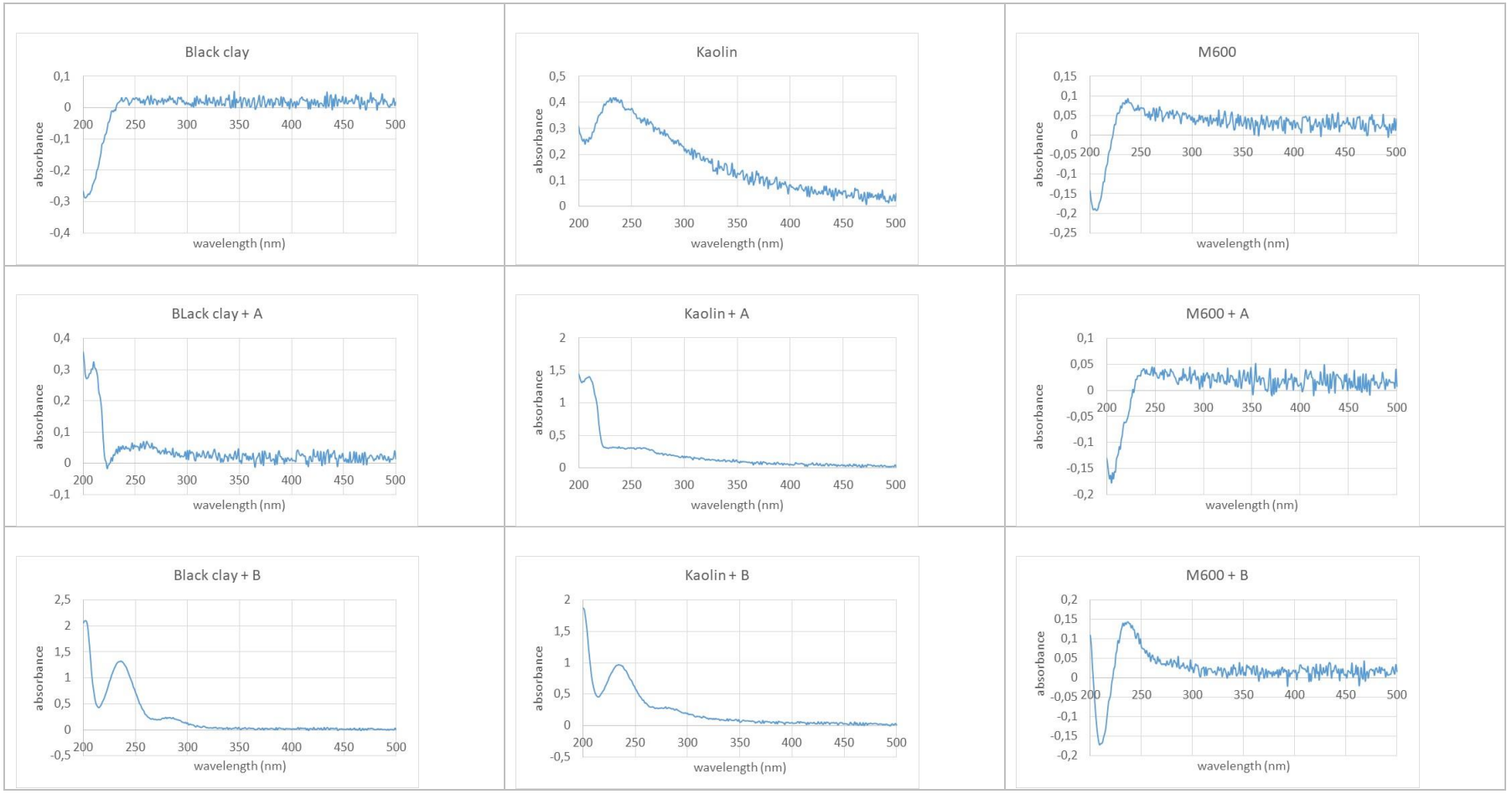
One of the important parameters in the choice of a suitable surface modification, is that the modification should be stable in water. It wouldn't be acceptable if desorption of the silane would occur, as this not only may reduce the adsorption capacity for the pharmaceutical, but would also result in the presence of silanes in the wastewater. Therefore, it was important to study the behavior of modified carrier material in aqueous dispersions.

The effect of this modification with Silane was tested in desorption experiments. The carrier materials Kaolin SL-55, Black Clay, M600 and M6000, modified with 1 % or 3 % of silane A, B or C (100 mg) were used. First it was determined whether the coupling of the silanes to the surface was reversible, resulting in desorption in water. If materials would desorb from the surface this could mean two things:

- The coupling is reversible, and silanes are desorbed upon dispersion in water. As a result of this the material would be unsuitable for water treatment purposes, as not only it cannot give a stable surface interaction between pharmaceutical and silane. In that case application of the adsorbent would result in an additional water contamination.
- The material contains unreacted silanes, that are adsorbed at or in between the coupled silanes. In this case they may compete with pharmaceuticals for adsorption sites at the carrier surface.

Both effects are unwanted.

The results of desorption experiments with Kaolin, black clay and M600, modified with either 3 % of silane A, B or C, are shown in Figure 8.


Black clay
absorbance
wavelength (nm)
Kaolin
absorbance
wavelength (nm)
M600
absorbance
wavelength (nm)
BLack clay + A
absorbance
wavelength (nm)
Kaolin + A
absorbance
wavelength (nm)
M600 + A
absorbance
wavelength (nm)
Black clay + B
absorbance
wavelength (nm)
Kaolin + B
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M600 + B
absorbance
wavelength (nm)

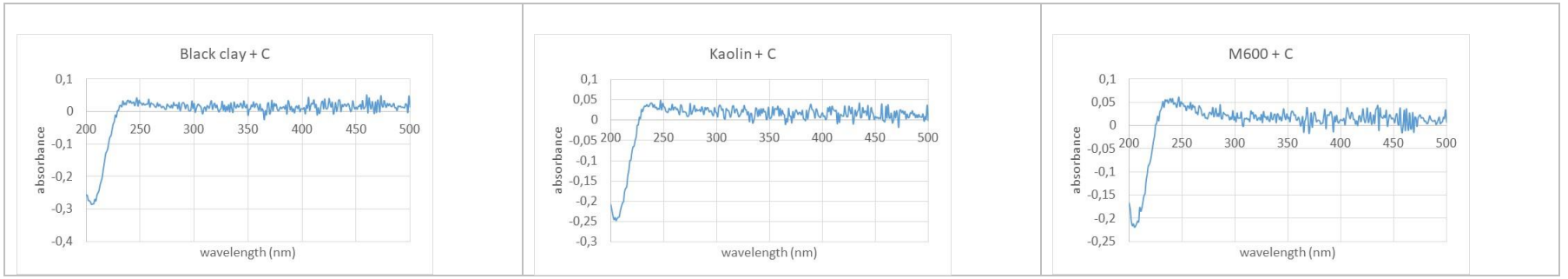

Figure 8: Desorption experiments with kaolin, black clay and M600, modified with 3 % of either silane A, B or C (see Table 2).100 mg of each sorbent in 20 mL of MilliQ water stirred over night and subsequently filtered. If silanes were present in the aqueous phase, this would result in an absorbance of the aqueous phase, as the silanes y absorb radiation of a wavelength between 200 and 500 nm.

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From the results shown in Figure 8 it was concluded that unmodified carrier material don't show any desorption of compounds in water. Furthermore, Silane C seems to give the least desorption in the 200-400 nm range, and that in general M600 as a carrier material seems to show less desorption than Kaolin or Black Clay, Therefore it was decided to carry out further desorption experiments with M600 and also M6000, which has a little larger specific surface area (5 m^2/g instead of 4.2 m^2/g). The results of the second series of desorption experiments are shown in Figure 9.

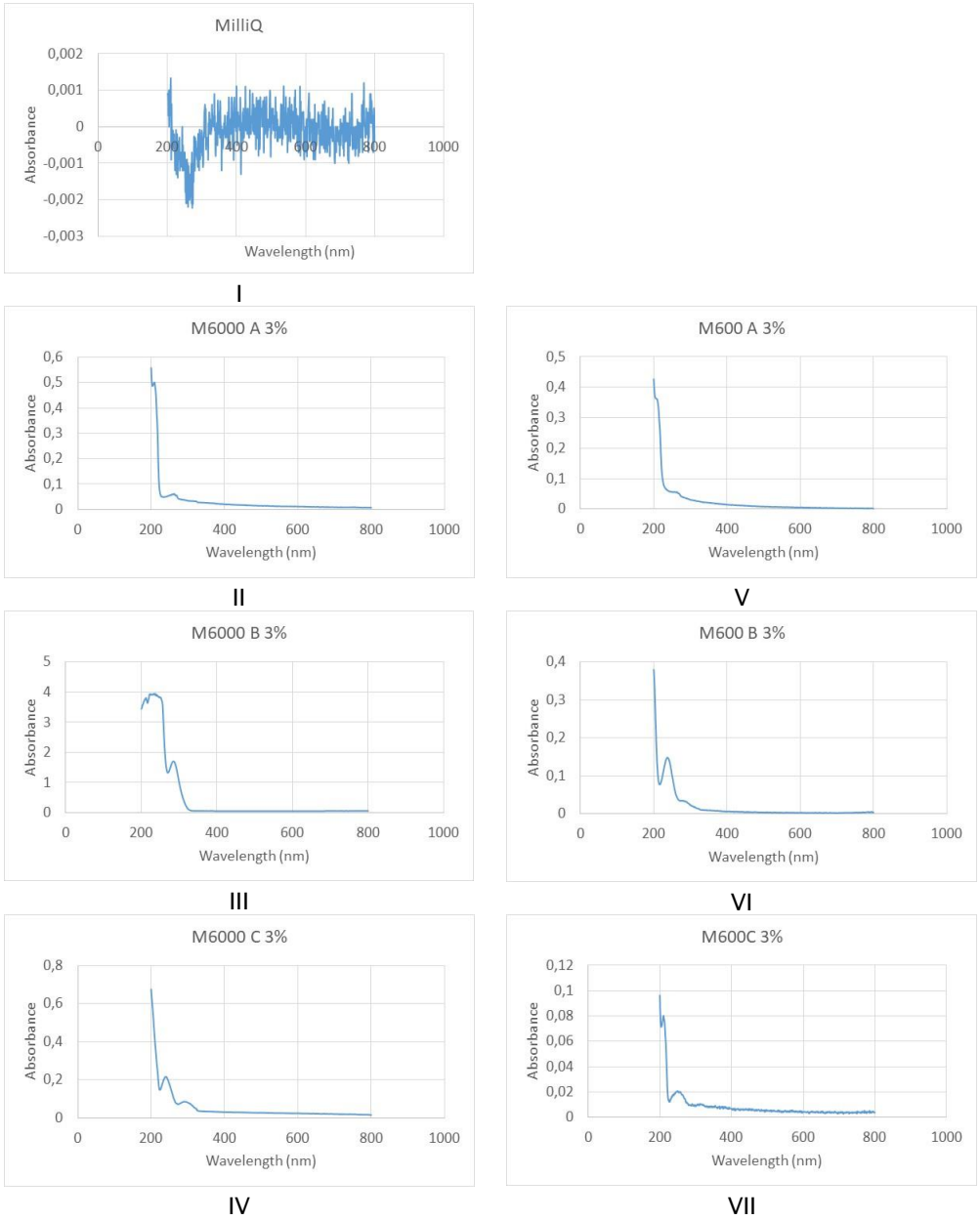


Figure 9: UV spectra of water after dispersion of modified carrier material. (IA) spectrum of Milli-Q water, II M6000 + silane A, II M6000 + silane B, III M6000 + silane C, V M600 + silane A, VI M600 + silane B, VII M600 + silane C

It was found that leakage of silane from the carrier surface occurred especially for the silanes B and C, which show a distinct UV absorption at about 250 nm. interfering with the adsorption experiments. The benzene ring in general gives a signal at about 250 nm, which is seen in silane A (very small signal) and in B. Silane C shows an absorption at about 240 and 290 nm.

As adsorption experiments indicated that the specific surface area of these adsorbents may be too small to obtain sufficient adsorption capacity, Ankerfume M25, an aluminosilicate with a surface area of about 20 m^2/g, was modified with silanes. For the surface modification 10 or 15 % of silanes was applied. As mentioned in paragraph 3.2 the modified material was washed with either methanol, 1-butanol, 2-propanol, DBE, water/methanol and water. Desorption experiments were carried out with all materials, and the results are shown in Figure 10.

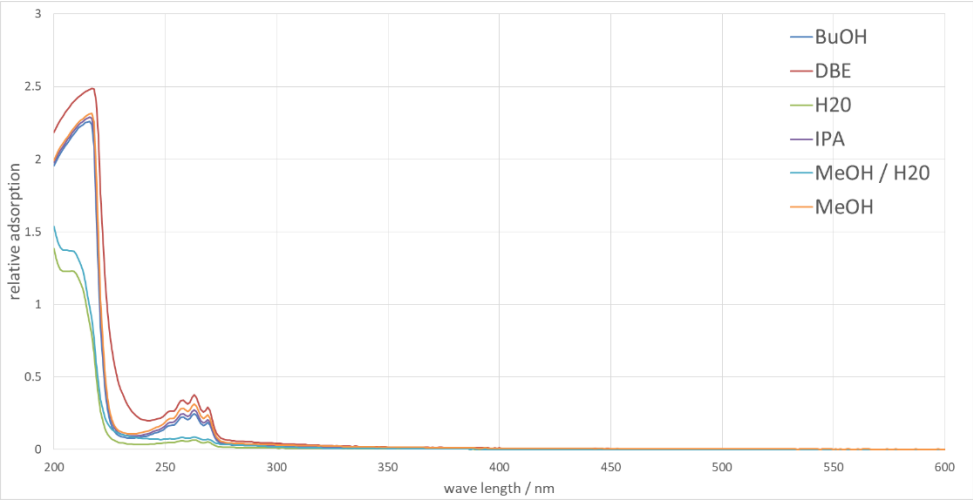


Figure 10: Desorption experiments with Ankerfume modified with silane C, and washed with different solvents

From these experiments it was concluded that in all cases no or only a negligible amount of silane was desorbed from the Ankerfume surface after washing.

4.2.1 TGA results

Thermogravimetric curves of unmodified, small batch and large batch Ankerfume M25 are shown in Figure 9 and Table 7. For the modified Ankerfume M25 samples a significantly higher weight loss can be seen compared to the unmodified version. This can be attributed to the organic functional group that are immobilised on the surface of the mineral. The difference in weight loss between the modified and unmodified Ankerfume is used to calculate the amount of functional groups on the surface (7). In case of the small scale batch about 0.13 mmol/g functional groups are immobilised on the surface of the material and in case of the large scale batch about 0.16 mmol/g functional groups are present. Assuming that every functional group interacts with one molecule of diclofenac, the maximum adsorption capacity of the material would be 56 mg/g for the small scale batch and 63 mg/g for the large scale batch.

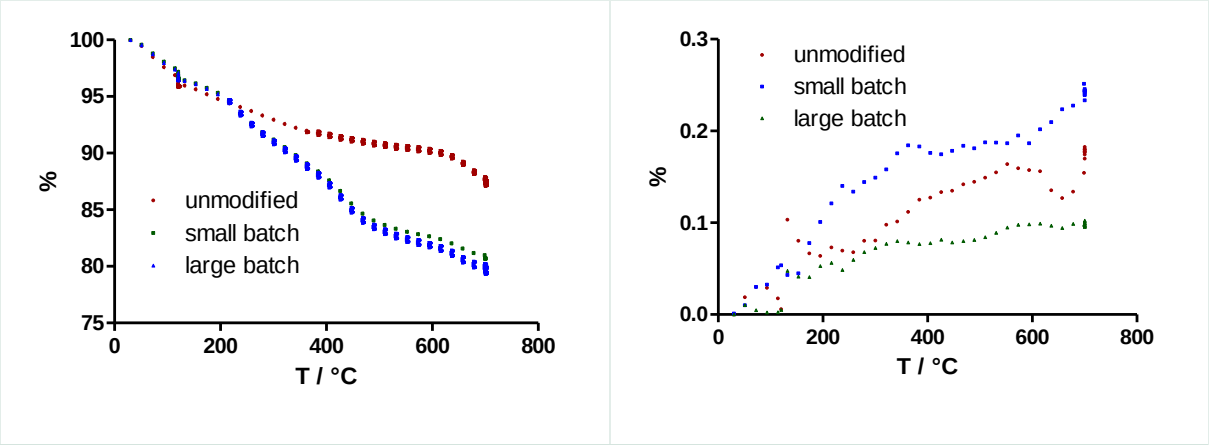


Figure 11: Thermogravimetric curves of the unmodified and two modified Ankerfume M25 adsorbents I). Standard deviation for the twofold measured curves (II).

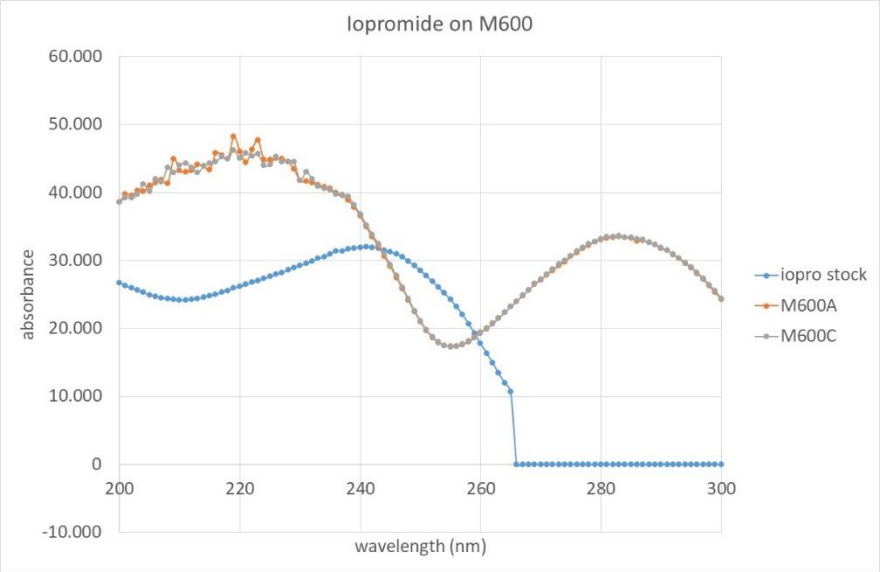
Table 7: Mass loss of the unmodified and the two modified Ankerfumes translated into amount of functional groups on the surface.

	Mass loss per g	Difference (g/g)	mmol/g	Max. ads. Capacity for diclofenac mg/g	SD mg/g
Unmodified	0.13	n/a	n/a	n/a	n/a
Small batch 1	0.19	0.07	0.19	56.08	0.04
Large batch 2	0.20	0.08	0.21	63.05	0.11

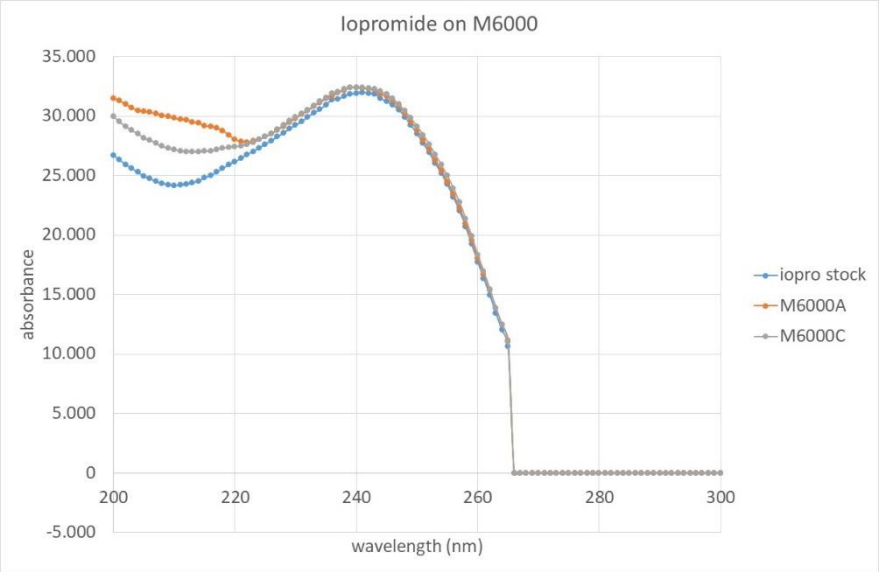
4.3 Laboratory adsorption experiments

4.3.1 First scan of possible interactions

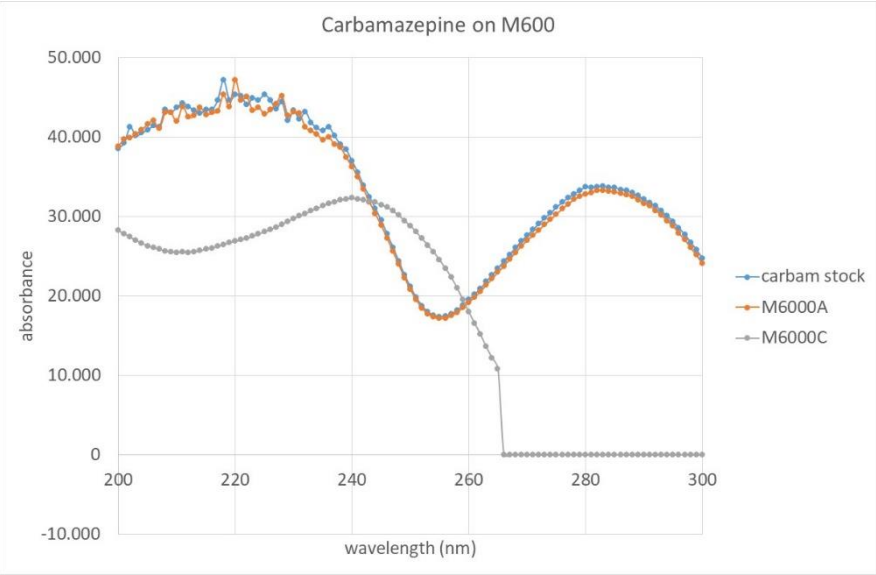
In order to obtain an indication of the effectiveness of interaction between adsorbents and pharmaceuticals, adsorption experiments were carried out in which the removal of the pharmaceutical from the aqueous phase was determined by measuring the UV-absorbance of the aqueous phase before and after addition of the adsorbent. First experiments were carried out using M600 and M6000 as carrier materials, modified with 3 % of silane A or C, as these, contrarily to silane B, had been shown to give no UV-signal in water (see Figure 9). The results of these experiments are shown in Figure 12.


Iopromide on M600
60.000
50.000
40.000
30.000
20.000
10.000
0
-10.000
absorbance
200
220
240
260
280
300
wavelength (nm)
iopro stock
M600A
M600C

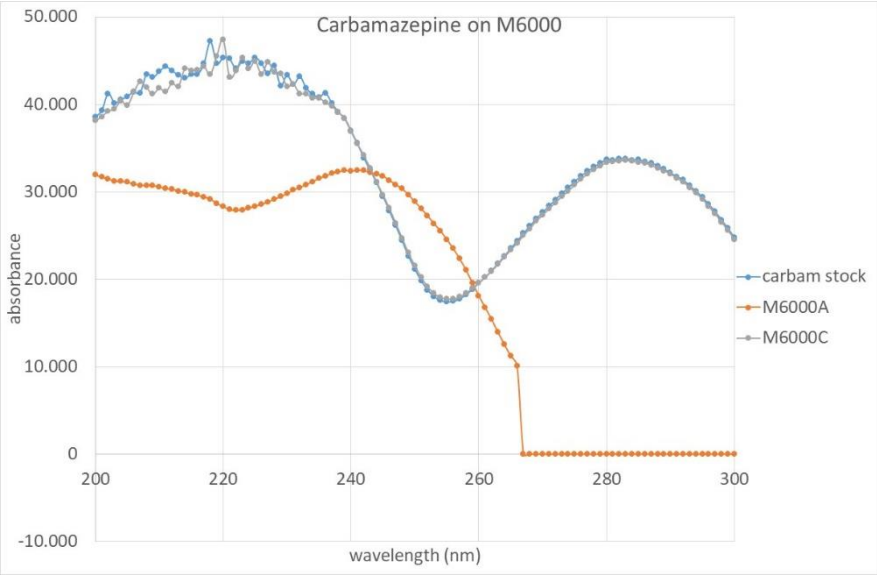
I


Iopromide on M6000
35.000
30.000
25.000
20.000
15.000
10.000
5.000
0
-5.000
absorbance
200
220
240
260
280
300
wavelength (nm)
iopro stock
M6000A
M6000C

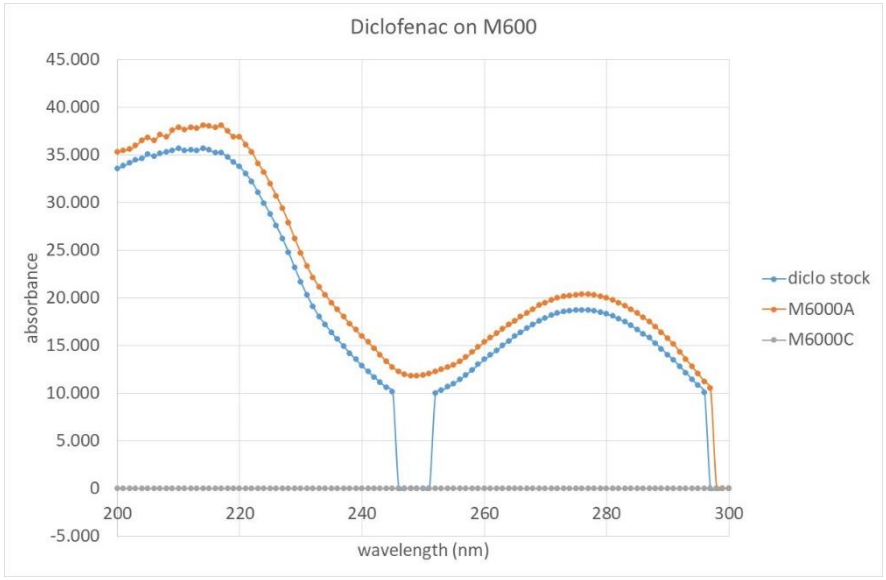
II


Carbamazepine on M600
50.000
40.000
30.000
20.000
10.000
0
-10.000
absorbance
200
220
240
260
280
300
wavelength (nm)
carbam stock
M6000A
M6000C

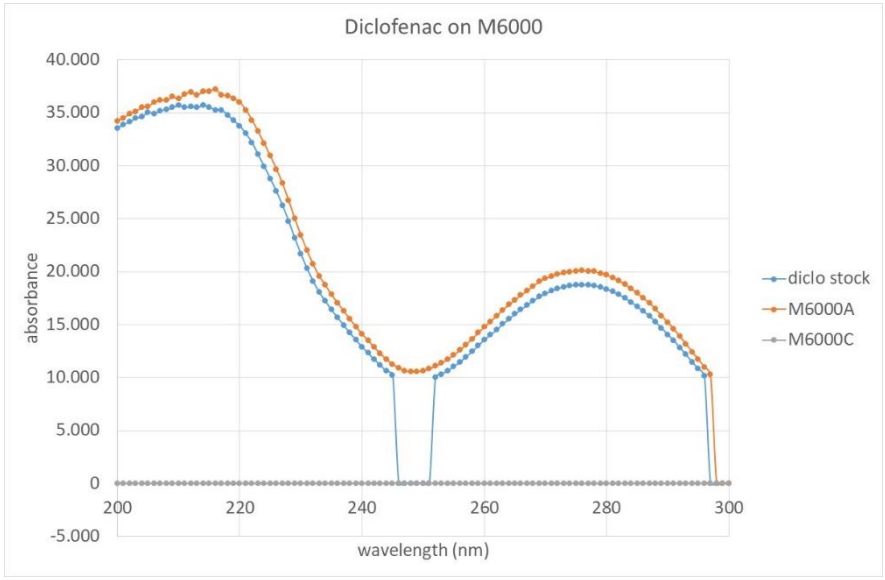
III


Carbamazepine on M6000
50.000
40.000
30.000
20.000
10.000
0
-10.000
absorbance
200
220
240
260
280
300
wavelength (nm)
carbam stock
M6000A
M6000C

IV



V



VI

Figure 12: UV spectra of solutions of pharmaceuticals before and after addition of an adsorbent. I M600 + iopromide, II M600) + iopromide, III M600 + carbamazepine, IV M6000 + carbamazepine, V M600 + diclofeanc, VI M6000 + diclofenac.

From these results it can be concluded that iopromide isn't removed by adsorption, neither by silane A or C. Also for Carbamazepine no significant removal can be observed. For diclofenac no removal is observed with silane A, but complete removal seems to be obtained applying silane C.

As it was expected that carbamazepine should be able to interact with silane A (the phenyl containing silane), it was suggested that possibly the surface area of M6000 was too small to see a good interaction. In order to check this assumption, silica, with a surface area of about 500 m^2/g, was modified with 15 % silane A or C and tested both with carbamazepine and diclofenac in Milli-Q water.

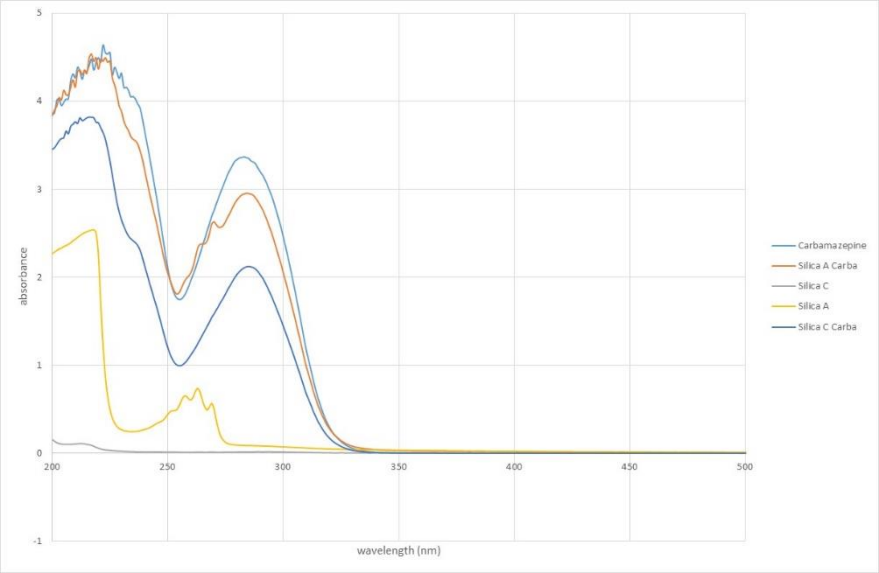


Figure 13: adsorption of carbamazepine on silica modified with 15 % silane A or C.

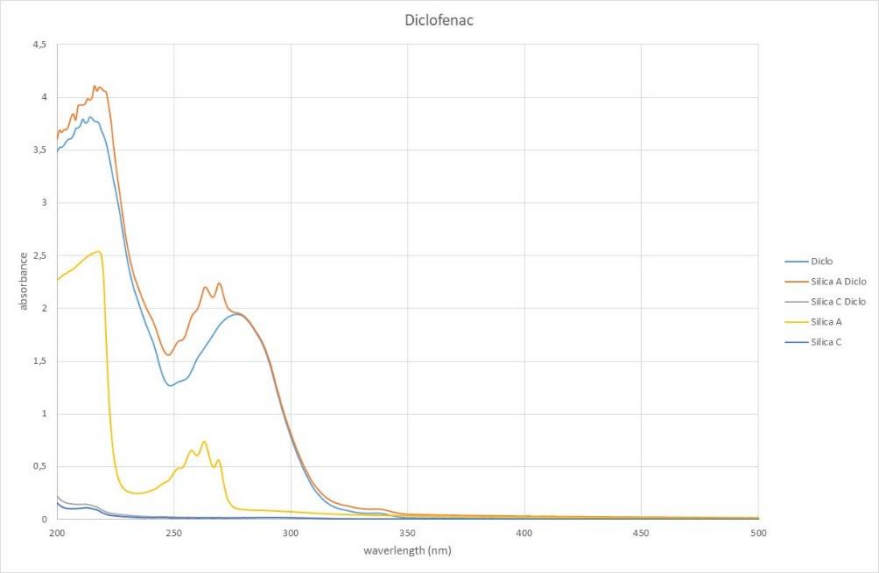


Figure 14: Adsorption of diclofenac on modified silica

From Figure 13 and Figure 14 it can be concluded that there is some leakage of silane A from the carrier surface, which is not observed with silane C. Figure 13 shows there is no significant adsorption of carbamazepine from the aqueous solution by silica modified with silane A, although the aqueous concentration of carbamazepine seems to decrease a little upon addition of silica modified with silane

C. Figure 14, however, shows almost all diclofenac was adsorbed by silica, modified with silane C. Silane A doesn't seem to interact with diclofenac.

Similar experiments were carried out with Ankerfume M25, modified with 10 or 15 % of silane C. The results are shown in Figure 15 and Figure 16. Experiments were carried out with about 15 mg of adsorbent

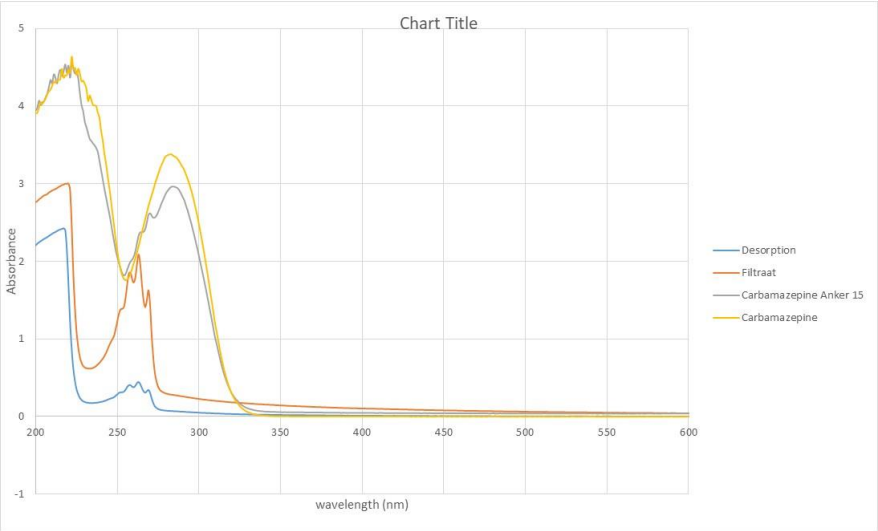


Figure 15: Adsorption of carbamazepine on Ankerfume M25, modified with silane A.

From Figure 15 it can be concluded that there is some signal of the silane A in the water, caused by desorption. It is clear that carbamazepine is not adsorbed by Ankerfume modified with silane A, as the signal of the carbamazepine solutions is almost identical to the signal of the solution treated with adsorbent.

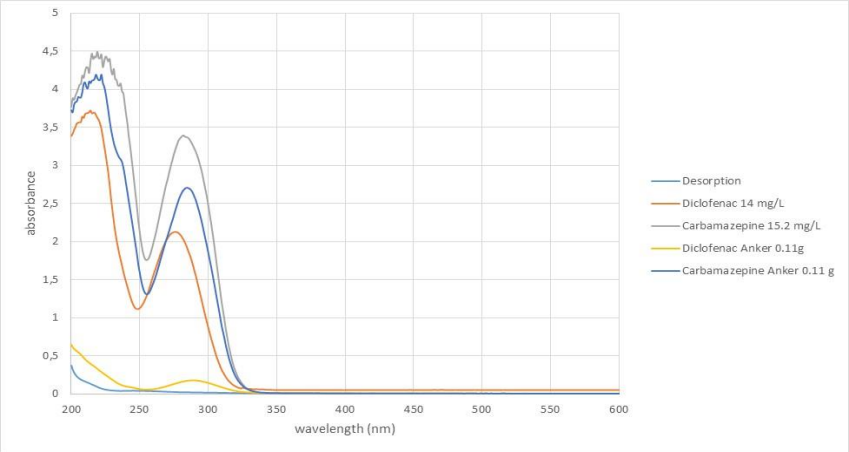


Figure 16: Adsorption of diclofenac on Ankerfume M25, modified with silane C 14 mg of diclofenac was dissolved in 20 mL, and 0,11 g of adsorbent was added

From Figure 16 it can be concluded that there is less desorption of silane C from the carrier material than of silane A (Figure 15). Diclofenac is almost completely removed from the water by this adsorbent, and carbamazepine is partly removed.

4.3.2 Sorption Interactions:

A solute can interact with a material and solvent in different ways. Interactions such as van der Waals, Coulomb, π-π interaction, and hydrogen bonding are the most important. Van der Waals interaction occurs between all molecules and functional groups, whereas π-π interaction is restricted to aromatic rings. Hydrogen bonding can occur between hydrogen donor groups, e.g. amines or hydroxyl groups and hydrogen acceptor groups, such as amines, hydroxyl, or ketone groups. Coulomb forces are electrostatic interactions between charged molecules and charged groups on a sorbent.

4.3.3 Determination of adsorption isotherms

It was tried to determine adsorption isotherms of carbamazepine, both in drinking water and in Milli-Q water. The results are shown in Figure 17.

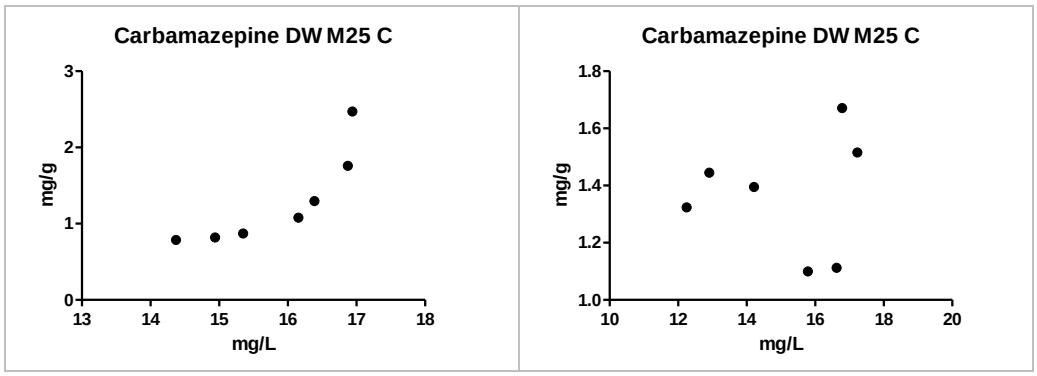


Figure 17: Adsorption of carbamazepine (a) on Ankerfume (b) modified with silane C in drinking water

The data in Figure 17 show that the results for carbamazepine seem unreliable (as they are scattered), which may be due to an instable adsorption.

Similar experiments were carried out with diclofenac in milli-Q water and in drinking water, as shown in Figure 18.

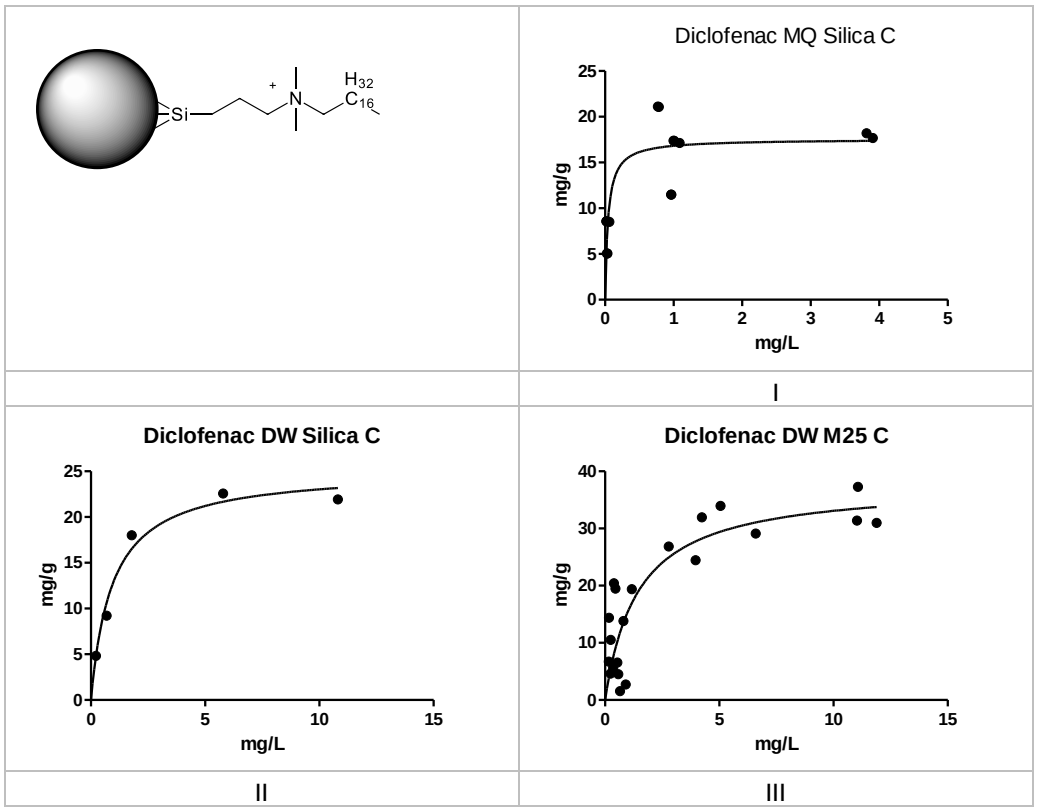


Figure 18: Adsorption of diclofenac on silica and Ankerfume in drinking water

Clearly, the adsorption capacity of Ankerfume M25 with silica C in drinking water (II) is higher than in milli-Q (I), which is remarkable, as milli-Q doesn't contain NOM whereas drinking water does. It would be expected that NOM might compete with adsorption sites at the particle surface, but the opposite seems to be true. Besides the adsorption capacity of the Ankerfume material appears to be significantly higher than that on silica (Figure 18, III versus II), which is remarkable because the specific surface area of the material is about 100 times smaller than the specific surface area of silica. An overview of adsorption capacities is shown in Table 8.

Table 8: Adsorption capacities of adsorbents for diclofenac.

	Milli-Q (mg/g adsorbent)	Drinking water (mg/g adsorbent)
Previous research silica modified with TBA*) (Hofman-Caris et al. 2015)	12	6
Silica + silane C	17	22
Ankerfume + silane C		40

*) TBA = tributyl ammonium chloride

The adsorption capacity of the adsorbent in drinking water is about 40 mg/g, which is in good accordance with the theoretical maximum adsorption capacity calculated in Table 7. This indicates that the principle of affinity adsorption, based on a specific interaction between surface group and pharmaceutical, works. Taking into account the theoretical maximum adsorption capacity calculated based on TGA results, these results indicate that about 65 % of the groups at the carrier surface can be covered with diclofenac. 100 % coverage maybe isn't possible, as it might result in steric hindrance of the adsorbed diclofenac molecules.

Although Ankerfume with silane C showed good results both in milli-Q water and in drinking water, it is important that sufficient adsorption capacity is reached in urine and wastewater too. Therefore, experiments were carried out in artificial urine. At first some problems were encountered due to crystallization of the artificial urine. Therefore, the artificial urine was diluted by a factor 1:5 for further experiments.

Adsorption of diclofenac in onto Ankerfume M25 C in MilliQ, DW, DW washed and artificial urine is shown in Figure 19.

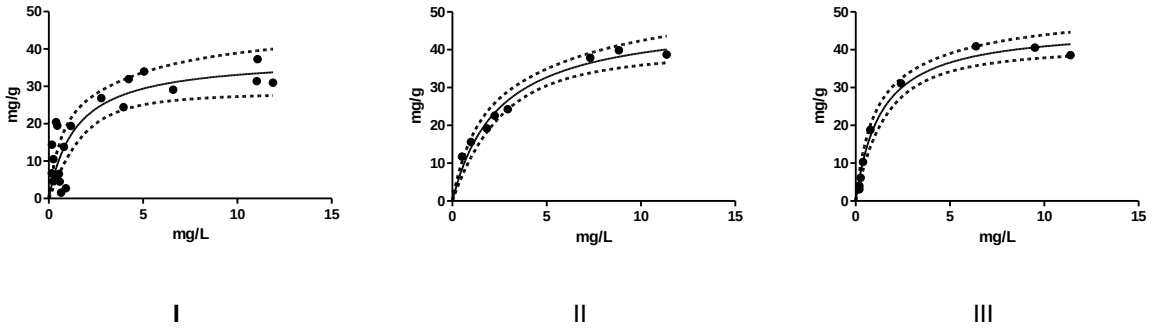


Figure 19: Adsorption of diclofenac onto Ankerfume M25 modified with 15 % of silane C. I adsorption in Milli-Q, II adsorption in drinking water, III adsorption in artificial urine.

It was found that in all three matrices diclofenac can be adsorbed quite well onto the particle surface, even in artificial urine. The composition of the matrix doesn't really seem to be of influence on the adsorption process, as was expected because adsorption is based on a specific interaction of the compound and the surface modification. Again a maximum adsorption capacity of about 40 mg/g was measured, which is in good accordance with the theoretical adsorption capacity of maximum about 60 mg/g (Table 7).

Based on the previous results it was decided to continue experiments with diclofenac, and some pharmaceuticals that also carry a negative charge, using silane C modification. Ten pharmaceuticals and one metabolite (2-hydroxy ibuprofen) were used. These are shown in

Table 4. The mixture contains seven carbonic acids, one amine, one amide and two amines/sulfonamines. A solution of the pharmaceuticals, including diclofenac, was used, and different amounts of adsorbent (varying from 2 to 500 mg to 250 mL of solution) were added.

Langmuir isotherms were received for 7 of the 10 compounds. The Langmuir isotherms can be seen in Figure 20 and Figure 21. The corresponding parameters are listed in Table 9. The sorption isotherms show that diclofenac adsorbs significantly better than all the other compounds, even better than all the other compounds combined. However, due to the limited amount of data points at higher concentrations for diclofenac, the uncertainty of the Bmax value is rather large. Also, it is obvious that only compounds that are negatively charged at pH around 7 show a tendency to adsorb. This is to be expected as the main interaction between the adsorption material and the compounds will be Coulomb forces in combination with van der Waals interaction. The better interaction of diclofenac compared to the other compounds can be attributed to Coulomb interactions between the positively charged adsorption material and the partial negative charge of the chlorine atoms in the 2,6 position of diclofenac.

However, the results clearly show that the principle of affinity adsorption also can be applied in (artificial) urine, and that competition by compounds present in urine don't really disturb the interaction. It also was found that other pharmaceuticals, negatively charged at pH 7, can be adsorbed. As a result of this the adsorption capacity for diclofenac seems to be a little lower than in the absence of these compounds (ca. 28 mg/g versus ca. 40 mg/g).

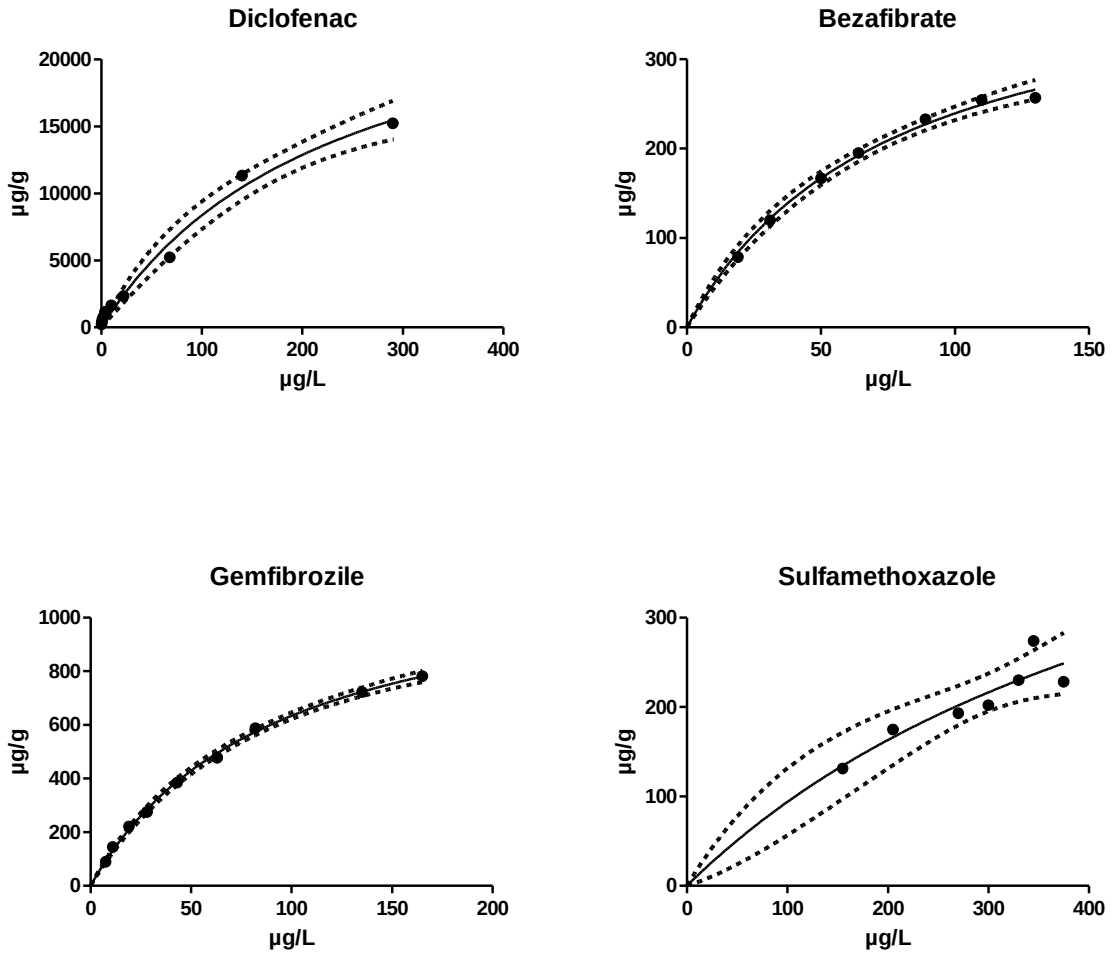


Figure 20: Langmuir isotherms for diclofenac, bezafibrate, gemfibrozile and sulfamethoxazole in artificial urine. 95 % confidence interval is shown dashed.

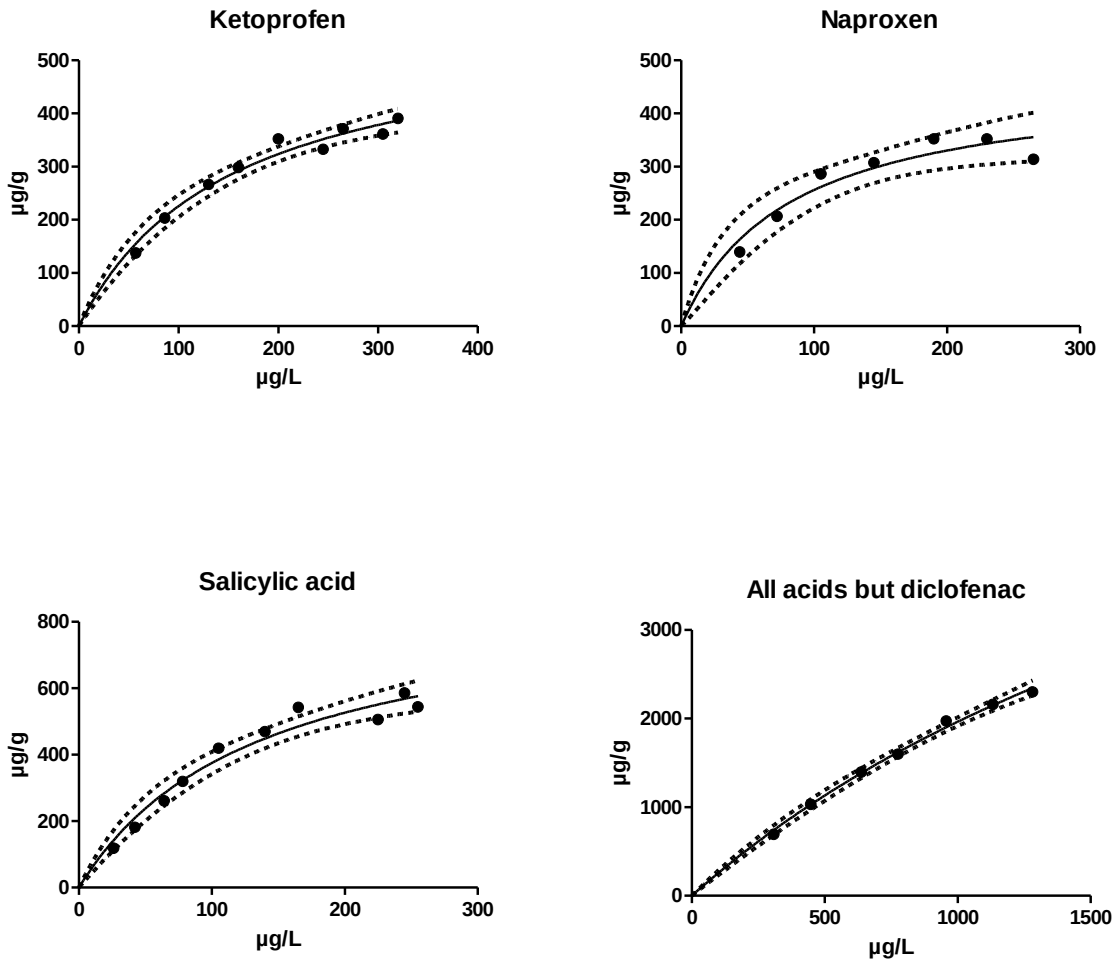


Figure 21: Langmuir isotherms for ketoprofen, naproxen, salicylic acid and all acids combined in artificial urine. Data acquired by mass spectrometry. 95 % confidence interval is shown dashed.

When the adsorption capacity is calculated in mmol/kg it can be seen that the total adsorption capacity is about 17 % lower in the mixture than in the solution containing only diclofenac. This may be due to spherical hindrance by relatively large compounds present at the surface.

Table 9: Maximum sorption capacity (Bmax) and sorption affinity (KL) of the sorption material for several pharmaceuticals in artificial urine.

Compound	Bmax (mg/kg)	K_L(mL/mg)	Max ads. Capacity (mmol/kg)
Diclofenac	27985 ± 4065	4.251 ± 1.16	94.50
Bezafibrate	423.7 ± 21.83	12.98 ± 1.1369	1.16
Gemfibrozile	1213 ± 36.65	10.94 ± 0.6576	4.83
Sulfamethoxazole	622.8 ± 306.7	1.774 ± 1.339	2.45
Ketoprofen	571.5 ± 44.06	6.526 ± 1.183	2.24
Naproxen	465.4 ± 54.77	12.23 ± 4.034	2.04
Salicylic acid	881.9 ± 91.48	7.4 ± 1.66	6.37
All compounds but diclofenac	7443 ± 950.8	0.3586 ± 6.150E-2	18.09
All compounds incl. diclofenac			112.59
Only diclofenac			135.07
theoretical			200

4.4 Pilot experiments

4.4.1 Pilot experiments at the hospital

As shown in section 3.10 in two nursing wards of the UMC Utrecht (D4 West and D5 West) all toilets were equipped with a container containing balls made of Ankerfume M25. Both patients and staff were asked to add such a ball to the toilet whenever they used the toilet. They didn't know it was unmodified material. Not only both nursing wards discharge onto the same sump (nr. 7), but also all other departments of the seven storey builing. Previous research had shown that the diclofenac concentration in the sump in general is low (< 1ng/L) ((Roex et al. 2016). Therefore, it was expected that it wouldn't be possible to determine a decrease in diclofenac concentrations when only two departments were using the adsorbent. Furthermore, it was thought that having to add a small ball would be easier for patients than having to add a spoon of powder.

4.4.1.1 General aspects

On Sunday afternoon (March 18th) all containers were placed at the hospital toilets for a pilot test of one week. It appeared that the containers used were suitable for this purpose. On Wednesday March 21st only one container had to be attached to the wall again, as it had partly come off. One container, on a toilet for disabled people, had been removed/fallen from the wall and placed on top of the cistern. On Sunday March 18th two containers could not be placed as the toilets had to be rebuilt on Monday March 19th . However, afterwards staff placed containers in both toilets.

It appeared that in the rinse kitchens there were two rinsing machines. On Sunday March 18th only one container had been placed, but on Wednesday March 21st in ward D4 West a second container and poster were placed.

4.4.1.2 Adsorption of diclofenac in sump

During the pilot trial water in sump 7 was sampled, and adsorption isotherms for diclofenac in this water were measured. The results are shown in

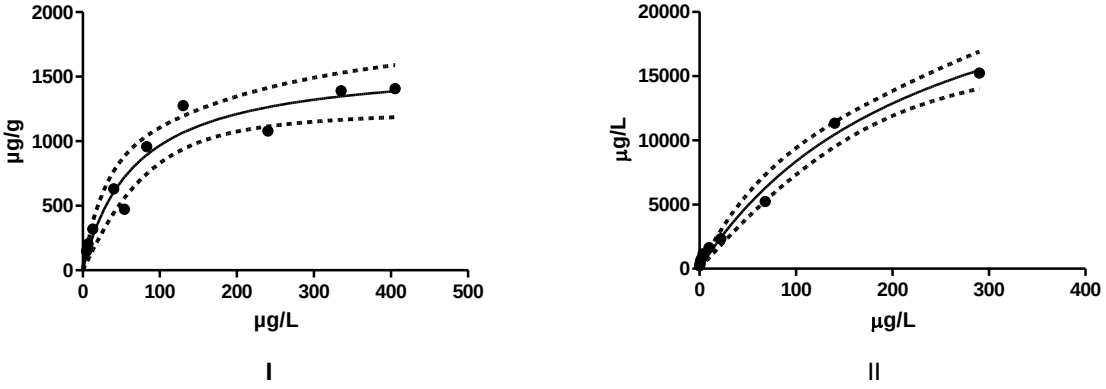


Figure 22 and Table 10. It was found that even in this complex matrix, containing organic matter and several contaminants (like naproxen and ibuprofen) from a mixture of wastewater, still an adsorption capacity for diclofenac of about 15 mg/g could be obtained. This is lower than the maximum adsorption capacity, but this can be explained by the presence of other charged compounds/pharmaceuticals in this sump.

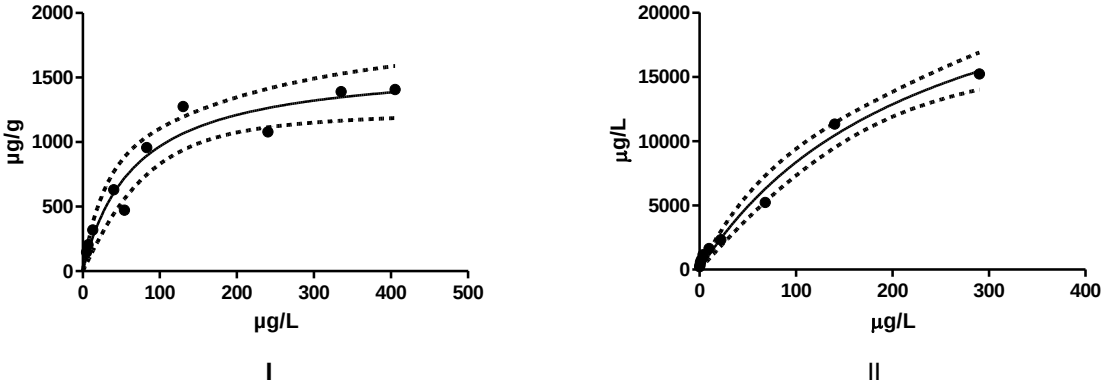


Figure 22: Langmuir isotherms for diclofenac in sewage from the university hospital in Utrecht (I) and in artificial urine (II). Data acquired by mass spectrometry. 95 % confidence interval is shown dashed.

Table 10: adsorption data in hospital wastewater and artificial urine

Hospital wastewater		Artificial urine	
Bmax (µg/g)	K_L (L/mg)	Bmax (µg/L)	K_L (L/mg)
1618 ±156.1	0.1488 ± 0.004507	27985±4065	0.004251±0.001116

4.4.1.3 Cooperation of patients and staff

The idea of the hospital pilot was that patients, staff and visitors would add some adsorbent (in this case a pellet) to the toilet before using it. Also people who didn't use pharmaceuticals were asked to do this, as the adsorbent in the wastewater would also be able to catch medicines from people who didn't use the pellets. In order to motivate people to cooperate, it was very important to inform everyone about the aim of the pilot, and the practical aspects. Especially staff had to be informed, as they were not only asked to cooperate themselves, but would also be the first point of contact for patients and visitors with questions. During two coffee breaks in the week previous to the pilot trial a presentation was given to the staff of both wards, to inform them about the goal of the project. It was found that in general hospital staff was not aware of the problem of pharmaceuticals entering the water cycle. However, after they had heard about it, most people said they would cooperate. It appeared that staff of D5 West was more aware of the goals of the pilot than the staff of D4 West. It might have been better to give the presentation at several coffee breaks, to reach more people.

When all containers and posters were installed at the toilets, people from the UMC and from KWR also told patients and their visitors about the goal of the project, and here too reactions in general were positive. Some people indicated that they thought it a good idea to do something about pharmaceuticals in wastewater. One patient was worried about people working at a STP because of the possible spreading of infections by wastewater. Several people indicated they would cooperate, which was confirmed by the decrease in the number of pellets in the containers during the pilot trial. In general patients said they considered it a small effort.

In the rinse kitchens many pellets were used by staff, indicating that the goal of the pilot was clear to many of them. In water the pellets quickly fell apart, but it was difficult to remove all material from the glassware. This had to be rinsed more often, thus increasing the amount of water required. This is a point of attention for the follow-up of the project and the practical implementation of the technology.

The mass of the containers, containing the pellets, was measured several times during the pilot period, and if necessary pellets were added. Based on the weights measured the amounts of pellets used could be calculated.

An overview of the numbers of patients per room and the total amounts of pellets used per room is shown in Table 14 and Table 15 in Appendix IV.

Figure 30 and Figure 31 in Appendix II show the total amount of pellets used by patients in different rooms

It can be concluded that there are large differences in use of pellets. However, it is very difficult to evaluate the use of pellets by patients and staff in detail, which is due to the following facts:

- There are rooms with 1, 2 or 4 beds. This accounts for a large variation in the number of people using one toilet. This may also vary during the course of the week, as not all beds will be used continuously.
- Some rooms/beds were not occupied by patients during the pilot week.
- Some patients only stayed for a short period.
- Some patients were not able to independently use a toilet. This may have been a significant part of the patients, as at D5 West 36 pellets were used in the rinse kitchen, and at D4 West even 216.
- During the first days not every po rinser in the rinsing kitchens was equipped with pellets, as a result of which the data of the rinsing kitchens don't apply to the full pilot period.
- At D4 west only during the last day of the pilot pellets were present in the staff dressing room. There were no pellets on other staff toilets

- The numbers of staff vary during day. This may also affect the use of pellets by staff in the staff toilets.
- The toilets for disabled people may be used by patients, but probably more by visitors.

The fact that so many pellets were used in the rinse kitchen indicates that staff really was aware of the importance of the pilot study. This also is reflected in the number of pellets used at the staff toilets: 85 at D5 West. During the week the total number of staff at D4 was about 155 and at D5 about 85. This might indicate that although staff was aware of the importance of trying to decrease the amount of pharmaceuticals in the wastewater, they probably didn't fully realize that it also may be important to use the pellets if you yourself don't use pharmaceuticals, in order to catch pharmaceuticals present in the wastewater. This is an aspect we should have explained better.

Furthermore, 3 pellets were used at the toilet for disabled people at D5 and 9 at D4. However, this may be related to the number of disabled people being present ad patients or visiting others. However, this indicates that also disabled people are willing to use the pellets. Previous to the pilot some staff were a little afraid that people with health problems shouldn't be bothered by environmental issues as well. However, our pilot showed that most patients were glad that in this way they could contribute to a better environment.

From the data shown in Table 15 however, it can be concluded that in total 275 patients used 450 pellets during this week, which is about 1.6 pellet per patient. This indicates that certainly both patients and staff are willing to cooperate and do something extra in order to protect the environment.

4.4.2 Pilot in the office building of Limburg Water Authority (WL) and Water Authority Company (WBL)

The office building of the WL/WBL consists of two parts, which are connected (see Figure 6 and Figure 23).

Figure 23: office building of WBL and WL in Roermond

In the oldest part, which discharges to the sump at the Kapelaan Sarsstraat, only offices are located. The newest part containing offices, meeting rooms and the restaurant, discharges onto the sump in the Maria Theresialaan.

General aspects

On Monday afternoon (May 21) all containers were placed at the 28 toilets in the old building and the 29 toilets in the new building. At the same time the information posters and score forms (including a ballpoint pen) were attached to the walls in prominent sight Figure 24.

The amount of adsorbent placed in a container in each toilet was weighed each evening of May 22, 23 and 24 to determine the amount used; at the same time the scores were counted and when needed the amount of powder was replenished, and weighed again.

Figure 24: Pilot investigation at WL/WBL in Roermond. Left: weighing the power for each toilet/container. Upper right: a tally sheet and the container with the powder and the small spoon. Lower right: sampling in the sump in the Kapelaan Sarsstraat (old building)

On Tuesday only one container had to be attached to the wall again, as it had come off. This toilet had not been used yet (no score on the tally paper and no powder used -checked by weighing). No further containers were detached during the rest of the pilot.

4.4.2.1 Adsorption of diclofenac in wastewater

Measurements were carried out the week before the pilot trial (May 15th and 17th) and during the pilot trial (May 22nd and 24th). For every day measurements were carried out two samples were prepared: one containing a mixture of the morning samples and one of afternoon samples. The results are shown in Figure 25. No components were dosed to the wastewater.

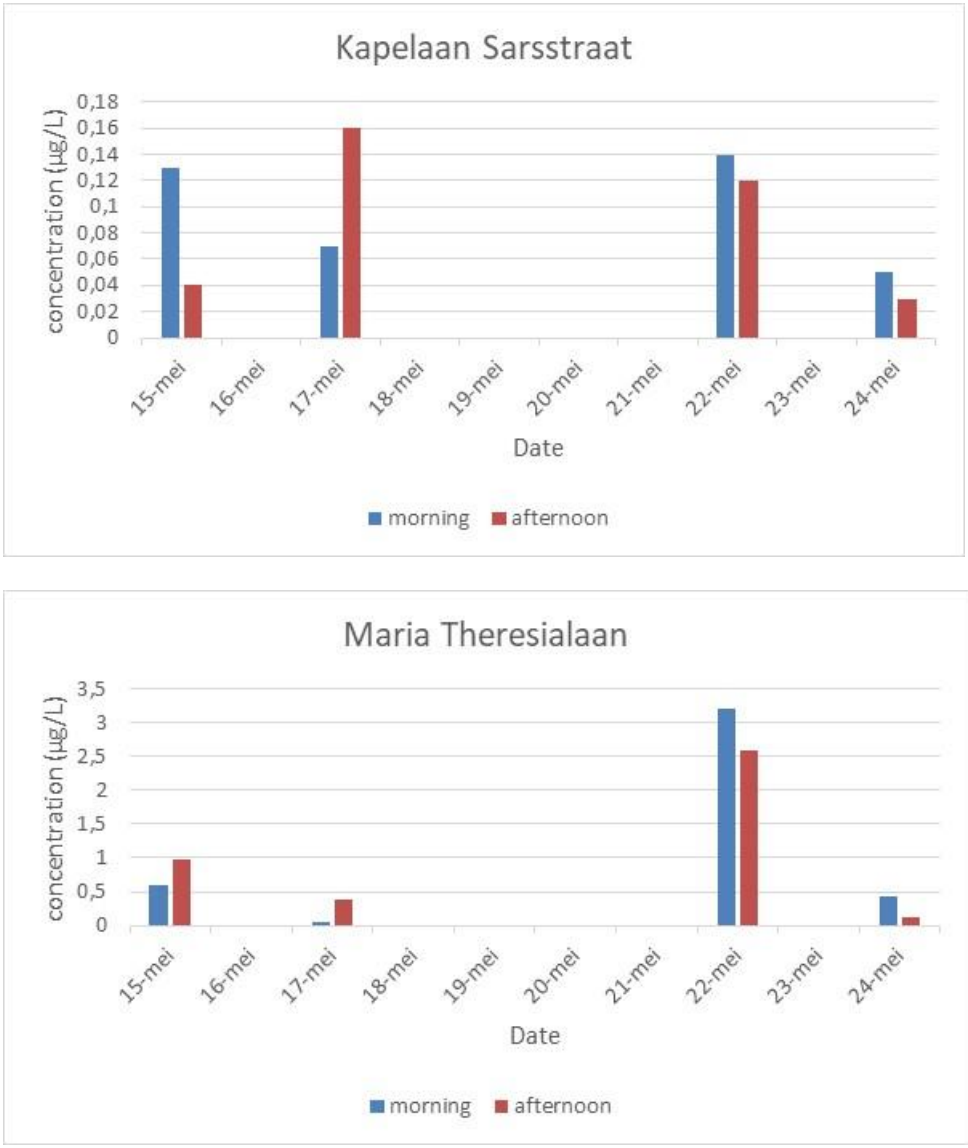


Figure 25: Presence of diclofenac in the sumps of Limburg Water Authority (Company). Upper figure data of the pit of the old part of the building, lower picture data of the pit of the new building.

From the data it can be concluded that diclofenac is used by people in the building, and that there is a large variation in diclofenac concentrations in the pit. Because of these variations it cannot be concluded whether the adsorbent really decreases diclofenac concentrations here, as the variations during a day and between days are very large. Where in the old building concentrations are in the same order of magnitude, on May 22nd in the new building a very high peak of diclofenac can be observed over the whole day. Because of this large variation, it cannot be concluded whether the adsorbent functioned properly in this wastewater One might speculate that a diclofenac user in the new building spilled a pill that reached the mixed sample, both in the morning and the afternoon.

However, the experiments showed that the wastewater of an “average” office building contains diclofenac in concentrations which were similar to the concentrations used in our laboratory experiments.

4.4.2.2 Cooperation of employees

In contrast to the hospital, the people in the office building already did realize that pharmaceuticals end up in the wastewater and surface water after use, because the Water Authority (Company) has been involved in research on the fate of pharmaceuticals for several years. In the week before the experiment all people in the building were informed trough the bulletin board on the intranet of both organizations. Also the cleaning staff was informed separately and asked to leave the containers be. This was also an opportunity to inform them of the purpose of the experiment.

The reactions were very positive, and people indicated they were willing to cooperate in this pilot. In the actual week of the experiment the cleaning staff was able to see the weighing and replenishment, which give cause for questions and answers. No disturbance of the materials was noted during the pilot. After the pilot week many employees informed after the results because they were curious. Alas, these were not available on such short notice.

A little spoon was provided, which would contain about 1 ml of powder, corresponding to 1,86 g of adsorbent. This amount was thought to be sufficient to catch all diclofenac excreted by a person taking the medicine. However, such a spoon is rather small, and a spoon with a longer handle would be easier to use.

The people who indicated they went to the toilet on average used 1.9 g of adsorbent, which corresponds very well with the average weight of a spoonful of adsorbent. However, it doesn't indicate which part of the employees indeed used the adsorbent, as it cannot be assumed that all people indicated they used the toilet. Some people indicated they forget to use the adsorbent, but did not keep score either.

It was found that the material gets stuck to the ceramics and metals in the toilets and urinals. Therefore cleaning requires extra efforts, as shown in Figure 26.

Figure 26: Adsorbent attached to ceramics and metal. Left and middle picture before cleaning, right picture after cleaning.

This problem may be prevented by adding the adsorbent in a dispersion with e.g. a surfactant. However, the effect of the surfactant on the adsorption capacity will have to be determined. This will be discussed in the following section.

4.5 Dispersion experiments

From the pilot trials it had become clear that the adsorbent attaches to glass and ceramics, which may hinder its acceptance by people. Applying the adsorbent in the form of a dispersion might solve this problem, but in order to obtain a dispersion of the adsorbent in water a surfactant will be required. This, in turn, might interfere with the adsorption of compounds on the particle surface.

In order to check this some experiments were carried out with two types of surfactant: the negatively charged sodium dodecyl sulfate (SDS) and the positively charged Cetyl trimethylammonium bromide (CTAB). The results are shown in Figure 27.

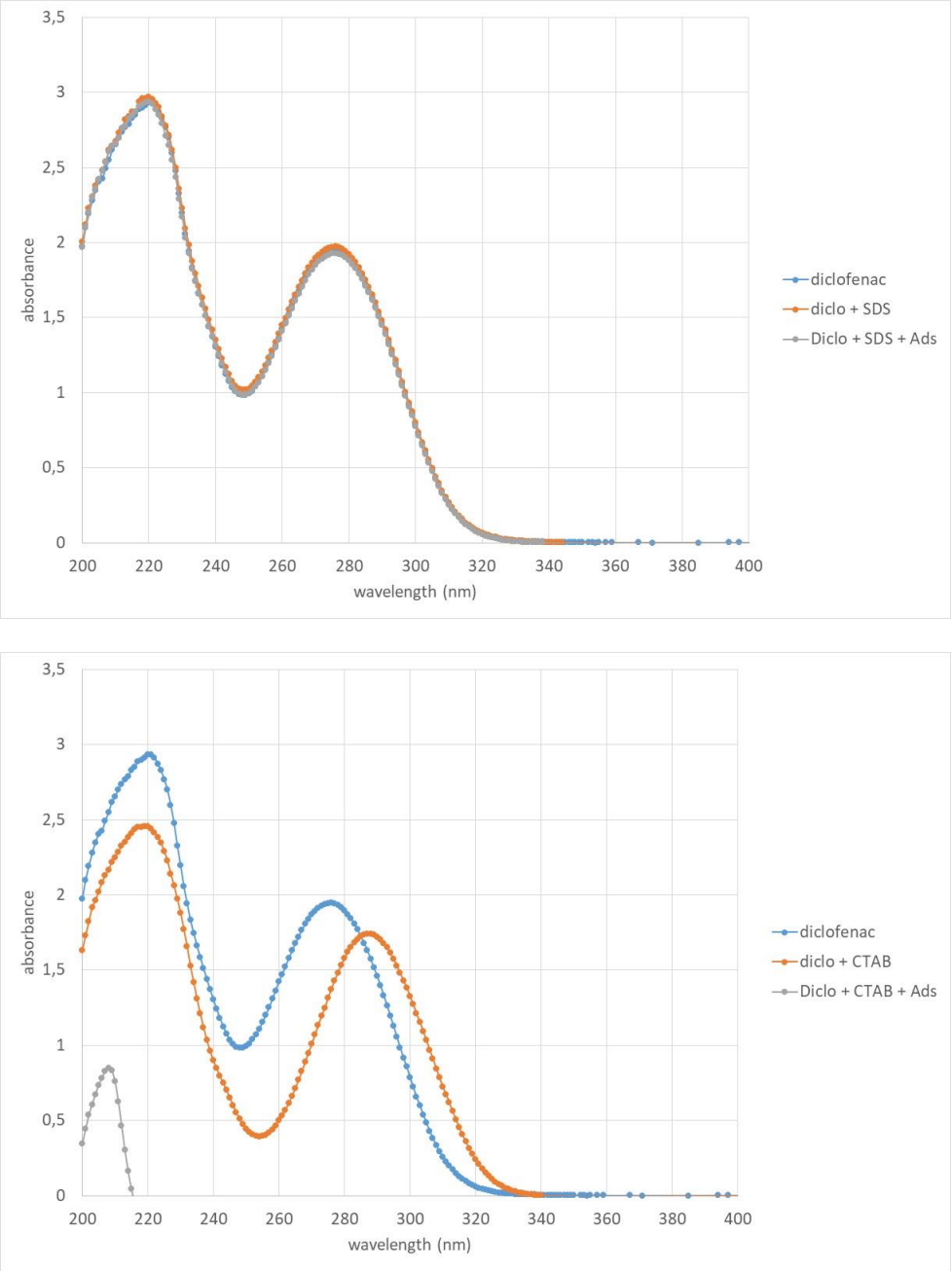


Figure 27: Effect of SDS (upper figure) or CTAB (lower figure) on diclofenac adsorption

Obviously, the presence of SDS doesn't affect the absorbance spectrum of diclofenac. However, it does prevent all adsorption of diclofenac at the particle surface, as no difference in absorbance spectra can be observed in the presence of SDS. For CTAB a different result was obtained. Theoretically it should be possible that the positively charged CTAB "complexes" with the negatively charged diclofenac, which is reflected in the (slightly) lower absorbance curve for diclofenac in the presence of CTAB. However, in the presence of the adsorbent almost all diclofenac seems to have disappeared from the water phase, indicating that diclofenac was removed by the adsorbent and that the presence of CTAB didn't affect that removal.

Although the dosing form still will have to be optimized, these experiments showed that adding a negatively charged surfactant will decrease the adsorption capacity. As positively charged surfactants may have a negative environmental impact, this topic still will require further research (e.g. looking for a positively charged surfactant with small impact, or a non-charged type of surfactant).

4.6 Recovery experiments

For the application of the adsorbents it is important that adsorption of diclofenac or other pharmaceuticals occurs quickly, and preferably irreversibly. In order to check the irreversibility of the adsorption process, adsorbent was loaded with diclofenac. Subsequently, the adsorbent was removed from the water phase by means of filtration, and again dispersed in water. After 5 and 15 hours the adsorption spectrum of the solution was measured. The maximum UV absorbance of the solution appeared to be 2,77. Subsequently 737 mg of adsorbent (Ankerfume M25 with 15% of silane C) was added to 980 ml of solution, decreasing the UV signal to -0.3. This indicates complete adsorption of the diclofenac. After isolation 360 mg of the loaded adsorbent was added to 490 ml of Milli-Q water. After 5 hours of mixing, the solution absorbance appeared to be -0,26, and after15 hours the UV signal was found to be -0,28. This clearly indicates that no diclofenac was removed from the adsorbent surface in clean water, and that the adsorption thus can be considered as irreversible.

4.7 Adsorption kinetics

An important parameter for the applicability of an adsorbent is the time required to obtain sufficient adsorption. If the adsorbent is going to be used directly in the toilet, it is important that adsorption is obtained before the mixture is diluted in the sewer system. Therefore the adsorption kinetics of diclofenac in drinking water were determined. The results are shown in Figure 28.

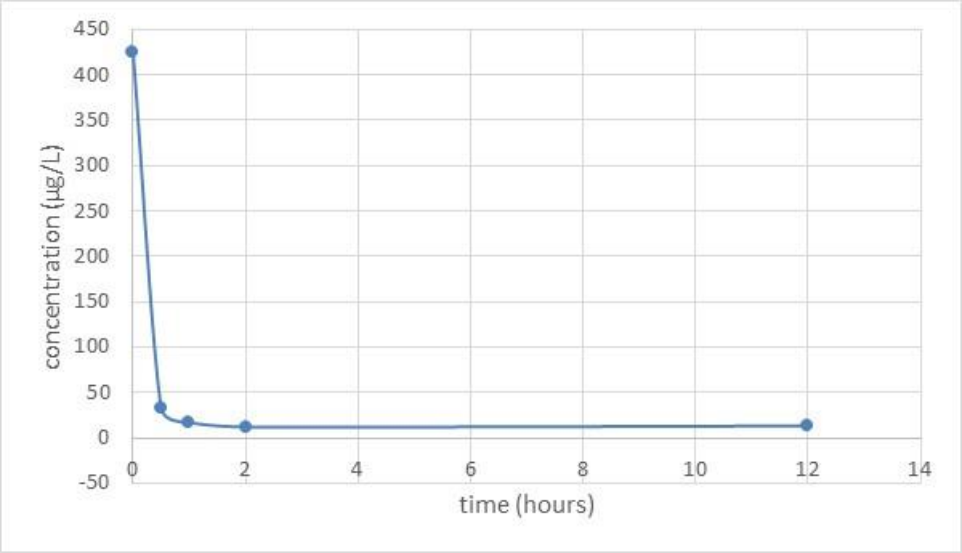


Figure 28: Diclofenac adsorption kinetics measurements in hospital wastewater.

From these data it can be seen that already at the first measurement after addition of the adsorbent almost complete adsorption was observed. As it will take some time to carry out the measurement, it wasn't possible to obtain data at an earlier stage than after about 10-15 minutes, but from these data it can be concluded that adsorption probably occurs almost instantaneously. which is advantageous for the application of the material directly in the toilet.

5 Practical application of affinity adsorption for the removal of pharmaceuticals from wastewater

5.1 Ideas for application methods

The adsorbents described in this report were designed for the removal of especially pharmaceuticals (in this case diclofenac) from wastewater, preferably directly in the toilet. In principle such adsorbents may also be applied in a sewage treatment plant, but that possibility was not taken into account within the framework of this project (although it doesn't mean in future such an application won't be possible). Especially water authorities have expressed their interest for application at a full scale WWTP, For dosing directly in the toilet handy dosage forms will be required, which can easily be used in houses, offices and hospitals. In Table 11 the following possible dosage forms are included and briefly explained below:

1. Modified toilet paper
2. Toilet cubes
3. Dispenser in cistern
4. "Tea bag" concept
5. Dispenser next to cistern (see Figure 29)

Figure 29: dosing system for surfactant at urinals in a Dutch hotel in Roermond (left) and in a hotel in South Africa (right)

Table 11: **practical forms of dosing adsorbents in the toilet**

Form	**Modified toilet paper**	**Toilet cubes**	**Dispenser in cistern**	**"tea bag"**	**Dispenser next to cistern**
Advantages	For sale at supermarket or pharmacy Little effort for user Application of a mixture of adsorbents possible Effective in sewer	For sale at supermarket or pharmacy Little effort for user Specific use in combination with pharmaceutical possible Application of a mixture of adsorbents possible Suitable for urinals Applicable by cleaning company Effective in sewer	Applicable by cleaning company Little effort for user Application of a mixture of adsorbents possible Effective in sewer	Distribution by pharmacy in combination with pharmaceuticals Directly applicable Already effective for dilution with rinsing water Mobile (can also be dosed at work, sports etc.)	Use existing system for new application Easy to install next to existing toilets Little effort for user Effective if first the dispenser is used before dilution with rinsing water Applying a mixture of adsorbents increases effectiveness in sewer Suitable for urinals
Disadvantages	Resistance to skin contact. Toilet paper is not always used during urinating, whereas most pharmaceuticals are excreted in urine Difficult with urinals	Medicine residues are always diluted by rinsing water, making cubes less effective	Adaptation of toilet required More suitable for new construction or replacement	Always co-operative action by user required	Always co-operative action by user required Incidental action required for replenishment

Practical feasibility	Not in the short term. Resistance from users because of skin contact	Sibelco has compacting methods that may be suitable for toilet blocks.	In the longer term feasible	Probably quick to realize	Dispensing system already exists Suitable medium still in development

Ad 1) Modified toilet paper

As the adsorbent consists of powder, it may be possible to process the material in toilet paper. The main advantage would be that people don't have to think of using an adsorbent. In principle the toilet paper can be issued in combination with a certain pharmaceutical. However, combinations of different adsorbents, for a wide variety of pharmaceuticals, can be applied, resulting in an universally applicable toilet paper. This may be implemented on a large scale, and for example may be sold in supermarkets. If it is applied by people who don't use pharmaceuticals themselves, it still may act as an adsorbent for pharmaceuticals present in the sewer system. Therefore, the toilet paper should be absolutely safe to use. However, there are no indications whether the carrier material may be toxic in any way. For large scale implementation co-operation with a toilet paper producer will be required. This is something that probably cannot be realized in very near future.

Application of modified toilet paper also has some disadvantages. Pharmaceuticals are mainly excreted in urine, but people don't always use toilet paper, especially not in urinals. The main disadvantage, however, is that people are reluctant to use modified toilet paper because of the skin contact. Large-scale acceptance therefore may be a problem.

Ad 2) Toilet cubes

Another method for "dosing" adsorbent close to the source is processing in toilet blocks. With each rinse, an amount of adsorbent is dosed to the water. Here too adsorbent may be dosed by people who don't use pharmaceuticals, but this will be an advantage, as the adsorbent also will be active in the sewer system. The toilet blocks may contain a specific adsorbent for a certain (class of) pharmaceutical(s), but also mixtures of adsorbents for a wide range of pharmaceuticals may be applied. The blocks can be sold by pharmacies or supermarkets. For individual use blocks are less convenient, as people cannot take the blocks with them to work, sports or restaurants. Therefore, the option with universal toilet blocks may be the most practical one. The adsorption capacity for specific pharmaceuticals may be lower in this case, but as more adsorbent will enter the sewer system the total removal may still be sufficient. As there is no skin contact, acceptance by the public will be less of a problem.

An additional advantage of this system may be that the combination of adsorbent with a surfactant in the toilet block may also solve the problem of adherence of the adsorbent material to ceramics and metal, by keeping the adsorbent in the aqueous phase.

For a large scale application co-operation of toilet block producers will be required

Ad 3) Dispensing system in the cistern

The use of an adsorbent dosage system in cisterns is more suitable for institutions such as hospitals, offices etc. A major advantage will be that people don't have to think about actively doing something, and that the dosing system may be filled by the cleaning team or company. The cistern has to be readily accessible, but the system in fact already exists (for dosing of e.g. cleaning and colouring fluid to the toilets). A large toilet manufacturer already indicated his company would be interested in producing such cisterns if they would be applied on a large scale.
As the adsorbent will have to be dispensed in the form of a stable dispersion, also the problem of adherence of the material to ceramics and metal will be solved.

For private use, this form of dosing may be relatively difficult to implement, as a different cistern will be required, or possibly the existing cistern will have to be adapted. Furthermore, sometimes houses don't have an easily accessible cistern.

Ad 4) "tea bag concept"
In the "tea bag concept", the patient receives a box of medicines from the pharmacy with a box of "tea bags" containing the complementary adsorbent(s) for the specific medicines. The main advantages of this form of dosing is that it is specific, that it can easily be taken anywhere and that acceptance probably won't be a problem. However, it does require active co-operation of patients. The bag should be made of a material that degrades quickly in the toilet, so that the adsorbent is released quickly and well distributed. A kind of toilet paper may be suitable for this. This concept probably can be realized in the short term.

Ad 5) Additional dispenser
In many African countries, but also in Dutch hotels, a cleaning fluid/ odor remover is added to the toilet from a separate dispenser next to the toilet (instead of in the cistern). It is often used to reduce the forming of chalk deposits in the toilet/urinal. This system may also be used for dosing adsorbents. This system is relatively easy to install next to existing toilets. In household use, the users have to supplement the reservoir themselves, and the application requires active co-operation of the users. The dosing dispersion may contain a specific adsorbent or a mixture of adsorbents. Furthermore, it will have to be a stable dispersion, probably stabilized by means of a surfactant, which will also solve the problem of adherence of the material to ceramics and metal.

The above list of possible forms of dosing of adsorbents is not exhaustive. Many variants and combinations are conceivable.

5.2 Consideration and choice

When considering the optimum dosing technology for large scale application, the following criteria are important:

- Efficiency of adsorbent.
  - Highest efficiency will be obtained when a relatively high concentration of the target compound is present, which is in the toilet, preferably before dilution occurs by flushing water.
  - Application of a specific adsorbent, aiming at one (class of) adsorbents versus a broad mixture, suitable for the removal of several (types of) pharmaceuticals.
- Ease of use.
  - For patients or the general public, and for cleaning people.
  - If specifically aiming at certain pharmaceuticals, it is possible for a patients to take the adsorbent with him?
  - Is the adsorbent also applicable in urinals?
  - Which (structural / technical) adjustments are needed to make it applicable in the existing situation?
- Availability and distribution of adsorbent by pharmacies or possibly supermarkets
- Safety. The adsorbent must be safe and hygienic to use (for example, no irritation on contact with hands or skin). It may not affect the existing infrastructure (toilet, urinal, sewerage, etc.).
- Acceptance by the user.

5.3 Future and follow-up questions

It is expected that in the long term the best results can be achieved by combining the various adsorbents in a toilet block, tea bag or dispenser emulsion to adsorb medicine residues in the toilet and/or sewer. They can be separated and processed in the STP. If specific pharmaceuticals will be targeted, distribution through pharmacies will be required, but if pharmaceuticals in general are targeted, the adsorbent may be sold by supermarkets.

For institutions, placing a dispenser in the cistern seems the best choice whether or not in combination with modified toilet blocks or tea bags for specific medicines. For private use, a distinction can be made between patients with long-term medication use and short-term use. For the latter group, the use of toilet blocks at home and tea bags for elsewhere may be preferred. For patients who use medication for a long time the use of modified toilet blocks is most practical, but placing a dispenser next to the cistern is also a good option for this group for home use. For outdoor use the use of tea bags is also the most attractive for this group of patients.
This also shows that in order to obtain the best possible removal efficiency, a combination of the previously mentioned dosage forms offers the best guarantee. However, the question still remains whether specific patients should be aimed at, or the general public.

More and more water authorities are considering an additional treatment step for STPs. Ideally, this would render the application of an adsorbent for the removal of pharmaceuticals unnecessary. However, it will still take a (long) time before this fourth treatment step will have been implemented on a large scale. Furthermore, it still is possible that certain pharmaceuticals will not be effectively removed by this treatment step, depending on the type of pharmaceutical and the technology applied. In such cases the use of this adsorbent may be complementary to the implementation of this fourth treatment step.

5.4 Alternative application

Within the framework of the present project only dosing to toilets was considered. The idea was that it would be more effective to remove pharmaceuticals directly at the source, where concentrations are high and the amount of different pharmaceuticals is relatively low. However, in principle there is no reason why the adsorbents shouldn't be applied at STPs. In this project it was shown that the material also effectively can adsorb pharmaceuticals from e.g. combined hospital wastewater. Therefore, application at a STP should also be considered.

6 Conclusions and recommendations

6.1 Conclusions

The following conclusions can be drawn from the results obtained within the project described in this report:

- Ankerfume M25 is a suitable carrier for adsorbents. This relates to physical properties, like particle size and density, and to chemical properties, like the possibility to chemically modify the surface. Furthermore, Ankerfume itself is non-toxic.
- Surface modification with silanes can be very effective, but it is important to rinse the material after modification, in order to prevent leakage of silanes from the particle surface during application.
- For diclofenac, and some other negatively charged pharmaceuticals, an effective adsorbent was designed, that has an adsorption capacity that is high enough to remove these pharmaceuticals from a toilet solution by applying about 1-2 g of material each time.
- For other types of pharmaceuticals an effective surface modification still has to be developed.
- Adsorption at the particle surface occurs fast enough (within some minutes) for application in the toilet.
- Significant adsorption of diclofenac can be obtained, even in a difficult matrix like artificial urine and real wastewater from a hospital or office building.
- The maximum adsorption capacity for the adsorbents prepared within this project was about 60 mg/kg, whereas in practice about 40 mg/kg was measured. Taking into account that the modification procedure had not been optimized, a coverage of about 65 % of the total surface groups is considered a good result. By optimizing the surface modification this may be improved.
- Pharmaceutical adsorption seems to be irreversible: no leakage of pharmaceuticals from the particle surface could be observed with the adsorbent produced in this project.
- The adsorption capacity of the adsorbent for diclofenac, developed in this project, is sufficient for practical applications. Addition of about 1-2 g of adsorbent would be sufficient for the removal of diclofenac present in a person's urine.
- The pilot trials, both at the hospital and at the office building, made people aware of the problem of the presence of pharmaceuticals in the environment. As a result they seemed to be willing to cooperate and use the adsorbent. This is true for office employees, but also for patients and hospital staff.
- Although the adsorbent shows good adsorption results, for dosing a practical solution will have to be found. Added as a powder. the material attaches too strongly to ceramics and glass. Dosing in the form of a dispersion might solve this problem. However, for a stable dispersion no negatively charged surfactant, such as SDS, can be applied.

6.2 Recommendations

- Still one problem that still needs to be solved is the dosing of the material for decentralized applications (in the toilet). Combination of the materials with a surfactant in a dispersion may be a solution, but the interaction between particle, surfactant and pharmaceuticals needs to be further investigated. Improved pelletization, or other dosing forms, (like a “tea bag”) also may be considered. More research is required to find the optimum dosing form.
- The possibilities for large scale application of the adsorbent at a full scale WWTP process should be evaluated. How much adsorbent would be required, and what implications would this have for the total process and further treatment of waste material?
- Different silane coupling agents should be investigated, to develop suitable adsorbents for other types of pharmaceuticals. For diclofenac the main means of interaction is Coulomb attraction, but for other types of compounds e.g. π-π interactions will probably be more suitable.
- It is important to bring the technology to the attention of a large audience (like policy makers, regional water authorities, medicine manufacturers etcetera). It also should be discussed how large scale implementation can be realized, e.g. by combining pharmaceuticals and adsorbent at the pharmacy, by making it available for general use, etc. This means pilot and demonstration projects will have to be carried out, and publicity on these projects should be generated, both for professionals as well as for the general public.

7 Acknowledgement

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Appendix I Data of Kaolin SL-S55

Kaolin SL-S5

Meissen, Germa

hnische Daten / Technical Data

Durch Hydrozyklonklassierung aufbereiteter Kaolin.
Lieferbar als lose genudelter Kaolin mit Kipp-LKW oder im Big Bag, als Standardvermahlung (< 500µm) ode
Feinstvermahlung (< 100µm) lose im Silo-LKW, 1 to Big Bags, in 25 kg oder 50 kg Papiersäcken auf Palette

Kaolin refined by hydro cyclone classification.
Available as noodles by tip lorry or big bag; as standard ground material (< 500 µm) or fine ground material (< 100 µm) by silo lorry; in 1 tonne big bags or in 25 kg or 50 kg paper bags on pallet.

Chemische Analyse / geglüht/ fired - %		**Chemical Analysis ungeglüht/ unfired- %**
SiO_2	65,2	59,0
TiO_2	0,5	0,5
Al_2O_3	30,0	27,2
Fe_2O_3	1,3	1,2
CaO	0,3	0,3
MgO	0,7	0,7
K_20	2,1	2,1
Na_2O	0,1	0,1
GV/ L.O.I	9,5	9,5
Kohlenstoff/ Carbon - ppm	< 3.000	

Mineralogische Zusammensetzung / Mineralogical Composition - %	
Kaolinitgruppe/ disordered Kaolinite	52
Glimmergruppe/ Mica (Sericite/ Illite)	17
Quarz/ Quartz	27

Die mineralogische Zusammensetzung wurde auf Grund der Daten der chemischen Analyse errechnet/ The mineralogical composition has been derived from calculations based on chemical analysis ed.

Korngrößenverteilung: Äquivalenter Kugeldurchmesser/ Particle Size Distribution: Equivalent Spherical Diameter

Mikrometer/ [µm] Micrometer	63	20	10	6,3	2	0,63
Durchgang/ [%] Undersize	100	96	90	78	52	32

Nassrückstand / Residue, wet screening

> 63 µm: 0,2 %

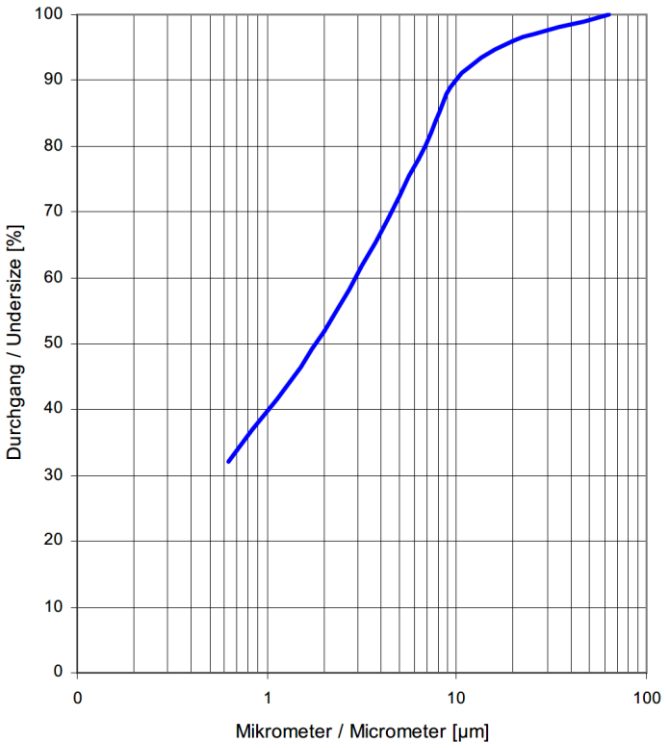
Trockenbiegefestigkeit/ M.O.R.
extrudiert Vakuum/ extruded vacuum

ca. 7,8 N/mm^2

he Daten / Technical Data

Meissen, Ge

Korngrößenverteilung / Particle Size Distribution



Technische Daten / Technical Data

Meissen, Germany

Wasseraufnahme/ Absorption of Water

trockengepreßter Prüfkörper/dry-pressed body 1240°C	ca. 2,22%

Gesamtschwindung/ Total Shrinkage

trockengepreßter Prüfkörper/dry-pressed body 1240°C	ca. 10,67%

Plastizität nach Pfefferkorn/ Plasticity - %

12 mm	ca. 58
16 mm	ca. 56
20 mm	ca. 54

Diese technische Auskunft hat nur indikativen Charakter. Alle Verkäufe erfolgen nach Muster und zu unseren allgemeinen Verkaufsbedingungen. April 2009

The technical data quoted on this sheet is indicative only. Any sale is by sample and is governed by our general conditions of sale.

SIBELCO DEUTSCHLAND

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Appendix II

Data on numbers of patients and pellets used at the hospital in Utrecht

Table 12: overview of numbers of patients and total amounts of pellets used per ward

Dept.	Room #	March 19th	March 20th	March 21st	March 22nd	March 23rd	Total # of patients calculated	Total # of pellets used	Pellets per patient
D4 west	18	2	2	2	2	1	9	3	0,33
	19	2	2	2	2	1	9	0	0,00
	20	1	1	1	2	2	7	1	0,14
	21	1	1	1	0	0	3	0	0,00
	22	1	1	1	1	1	5	0	0,00
	23	-	-	-	-	-	0	0	
	24	1	1	1	1	1	5	0	0,00
	25	4	3	4	3	3	17	13	0,76
	26	-	-	-	-	-	0		
	27	2	3	4	3	3	15		0,00
	28	2	2	1	2	2	9	25	2,78
	29	1	4	3	2	1	11	8	0,73
	30	4	4	1	3	2	14	5	0,36
	31	2	2	2	2	2	10	9	0,90
	32	1	1	1	1	1	5	0	0,00
	33	1	1	1	1	1	5	8	1,60
	34	0	1	1	1	1	4	0	0,00
	35	2	2	1	2	2	9	21	2,33
	Total #of patients calculated	27	31	27	28	24	137	93	0.68

	Total # of patients measured*)	31	30	34	30	32	157	93	0.59
	Rinse kitchen							216	1.97**)
	Toilet							9	
	Staff toilets							17***)	
D5 west	17	1	1	1	1	1	5	7	1,40
	18	1	1	1	1	1	5	3	0,60
	19	1	1	1	1	2	6	0	0,00
	20	2	4	3	4	4	17	0	0,00
	21	4	2	3	4	4	17	28	1,65
	22	2	1	1	1	1	6	16	2,67
	23	2	3	4	4	4	17	42	2,47
	24	2	4	4	2	3	15	1	0,07
	25	0	2	2	2	2	8	5	0,63
	26	1	1	1	1	1	5	0	0,00
	27	1	1	1	0	0	3	0	0,00
	28	1	1	1	1	1	5	0	0,00
	29	2	2	2	1	2	9	3	0,33
	Total #of patients calculated	20	24	25	23	26	118	105	
	Rinse kitchen							36	1.19**)
	Toilet							3	

	Staff toilets							128	

*) The number of patients per room at D4 West is a snapshot taken during day time. However, sometimes patients don't stay all day at the nursing ward, or arrive after the snapshot was taken, and thus it is possible that in total more patients were at the ward at a certain day. For D5 west we don't have the total number of patients, and it is not clear whether here too more patients may have been present.

**) The number of pellets used in the rinse kitchen also should be taken into account in the number of pellets used by patients.

**) This number of pellets was used in less than one day.

For D4 we don't have information on rooms 17, 25 and 26, and for D5 we don't have information on rooms 30-35. The use of pellets per room is shown in Figure 30.

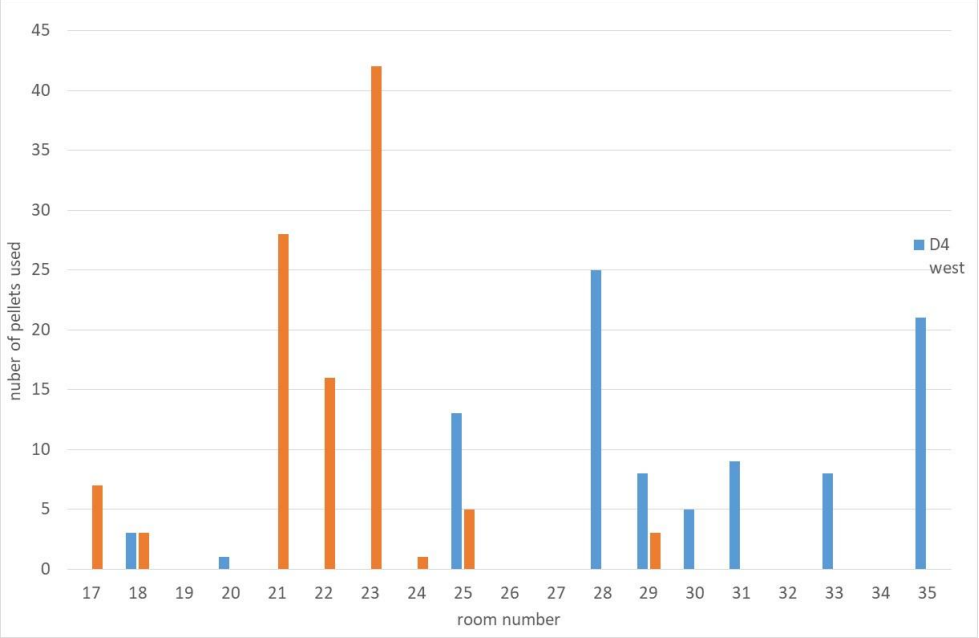
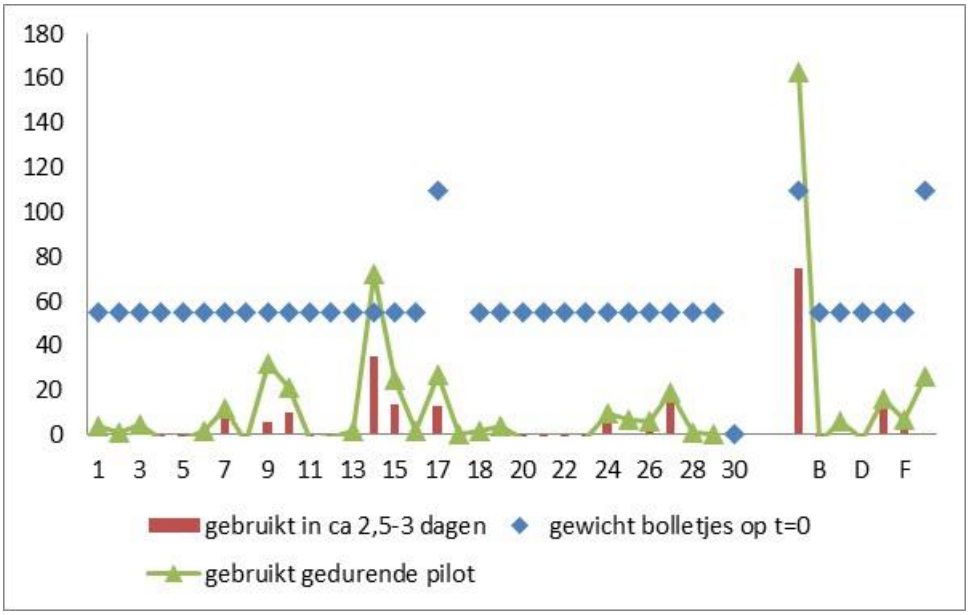


Figure 30: use of pellets by patients in rooms

Detailed results of pellet use during the pilot week are shown in Figure 31.



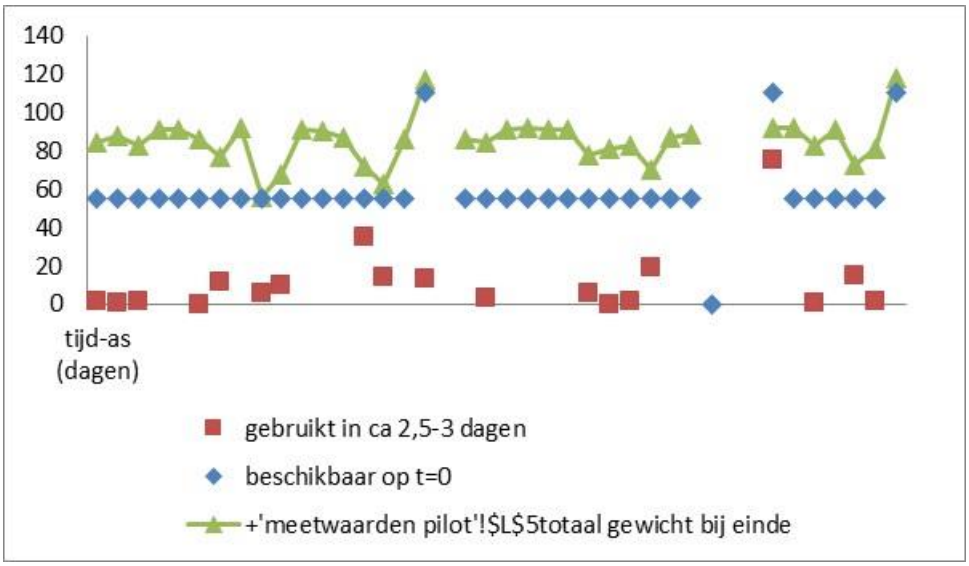


Figure 31: detailed use of pellets at both D4 and D5 during pilot week.

Appendix III

Adsorption kinetics

Table 13: diclofenac adsorption kinetics measurements with Ankerfume M25 + 15% silane C

Time (hours)	Adsorbent (mg/250 ml)	Concentration (µg/L)	Adsorbed (µg/g)
0	0	425	
0,5	324,8	33	301,7241
1	327,3	17	311,6407
2	322,6	12	320,0558
12	322,8	13	319,083

Appendix IV

Measurement data of pilot WL/WBL

Table 14: Diclofenac concentrations (µg/L) in pits of Limburg Water Authority -Company

	Maria Theresialaan		Kapelaan Sarsstraat	
	morning	afternoon	morning	afternoon
15-may	0.6	0.98	0.13	0.04
17-may	0.04	0.39	0.07	0.16
22-may	3.2	2.6	0.14	0.12
24-may	0.42	0.13	0.05	0.03

Table 15: data of pilot investigation at WL/WBL

		Tuesday		Wednesday		Thursday							
	Number		number		number		Number						
New building	WC's	gram	of visits	gram	pf visits	gram	of visits	% We/Tu	% Th/We	% Th/Tu			
Total	29	241	179	170	123	228	155	69%	126%	87%			
WC's Ladies	14	126	103	80	63	124	90	61%	143%	87%			
WC's Gents	7	51	34	49	30	53	25	88%	83%	74%			
Urinal	7	29	40	41	29	45	38	73%	131%	95%			
WC Invalid	1	35	2	0	1	6	2	50%	200%	100%			
	Number		Number		Number		Number						
Old building	WC's	gram	of visits	gram	of visits	gram	of visits	% We/Tu	% Th/We	% Th/Tu			
Total	28	532	306	445	248	356	182	81%	73%	59%			
WC's Ladies	10	176	133	157	96	104	69	72%	72%	52%			
WC's Gents	9	138	64	121	64	124	43	100%	67%	67%			
Urinal	8	176	102	144	81	110	65	79%	80%	64%			
WC Invalid	1	42	7	23	7	18	5	100%	71%	71%			
											Average dose		
								Total	Total		Tuesday	Wednesd	Thursday
	Number		Number		Number		Number		Number		gr pp	gr pp	gr pp
Both buildings	WC's	gram	of visits	gram	of visits	gram	of visits	gram	of visits		g/#	g/#	g/#
Total	57	773	485	615	371	584	337	1972	1193		1,6	1,7	1,7
WC's Ladies	24	302	236	237	159	228	159	767	554		1,3	1,5	1,4
WC's Gents	16	189	98	170	94	177	68	536	260		1,9	1,8	2,6
Urinal	15	205	142	185	110	155	103	545	355		1,4	1,7	1,5
WC Invalid	2	77	9	23	8	24	7	124	24		8,6	2,9	3,4